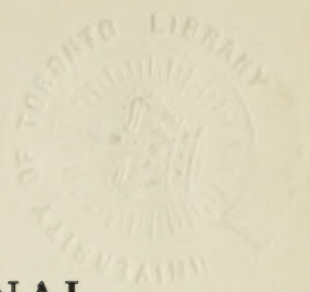


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AMERICAN JOURNAL OF DISEASES OF CHILDREN

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American Journal of Diseases of Children

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INTRODUCTION

The literature connected with pedology—the science of the child age—has undergone vast changes since Thomas Thacher's "A Brief Rule to Guide the Common People of New England How to Order Themselves and Theirs in the Small Pocks or Measles" (Jan. 21, 1677-78). This "Broadside," twelve inches by seventeen in size, has been followed by many more broadsides; indeed by roars of broadsides. "The History of American Pediatrics Before 1800," it is true, fills only twenty-five pages of *Janus*, 1902." It contains, however, mention of the previous and classical treatise of Samuel Bard, "An Enquiry into the Nature, Cause, and Cure of the Angina Suffocativa, or Throat Distemper, as it is commonly called by the Inhabitants of this City and Colony. New York, 1771."

The Nineteenth Century yields a long series of magazine articles and text-books. Dewees, Stewart, Eberle, Condie, Charles D. and Fordyce Meigs were physicians of fame, and their manuals were highly appreciated. Toward the end of the century (1889) W. V. Keating began his five volumes of a "Cyclopedia of the Diseases of Children," which has exerted a great influence in enhancing the taste for the study of healthy and diseased child-life, similar to what C. Gerhardt's epoch-making "Handbuch"—a modest title for a vast achievement—accomplished for Germany since 1877, and Grancher and Comby's "Maladies des Enfants" for France since 1898.

The first systematic instruction in pedology was furnished by the small New York Medical College in East Thirteenth street. In its reorganization of 1860, a full professorship was established. It carried the title of "Infant Pathology and Therapeutics." Subsequent imitations in later times and in other schools of medicine contented themselves with "Pediatrics," the *treating* of children, or the "Diseases of Children," only. The college closed its doors in 1864, during the blights of the Civil War. Meanwhile, the newly founded Bellevue Hospital Medical College organized in 1861 a "Clinical Professorship" for the diseases of children. In

that chair Dr. J. Lewis Smith displayed great industry and enthusiasm, and did much to enlighten the profession in regard to both the difficulties and the importance of the comparatively new doctrine. Another clinical professorship of the same nature was established in 1865 by the University Medical College, and in 1870 by the College of Physicians and Surgeons.

Since that time, the example given by New York has been followed by a large number of the medical schools in the country. Very few of them founded full professorships endowed with the full rights and duties awarded to the rest of the teachers who connected themselves with a medical school or the medical faculty of a university. Harvard was the first to see the light. Though the recognition came late and is far from being universal, we are still ahead of the present status of pedology in the curricula of most European medical schools. Germany, to this day, has few full professorships for instruction in the diseases of children. Indeed, its great teacher and classical writer, Eduard Henoch (1881) closed in 1893 his academic career with the title of a mere "Extraordinary Professor." When, a few weeks ago, however, he was taken away, 90 years old, he had the satisfaction of knowing that there was at last a breach in the short-sighted conservatism of German universities, and that at last a few full chairs of pedology had been established.

Great men like him are scarce in any part of medicine. To excel in close observation, logical reasoning, and elegant and precise diction, together with the faculty of teaching, is given to few men. Charles West in England (1848), Rilliet and Barthez in Switzerland and France (1843), belong to that class and deserve with Henoch the name of classical authors and instructors. They have passed away, but they have been followed by successors, few, it is true, of equal rank, but very numerous and many of them meritorious writers. If but few approach them, the multitude of those who have something to say—and the much greater multitude who say it anyhow—have made the study of the child and its diseases popular and interesting. If it so happens that too much is published, that is only a repetition of the experience of other doctrines in our science and art. Guttenberg's art could not have been discovered by everybody who is satisfied with utilizing or abusing it.

Our present copious pediatric literature dates from about the middle of the last century. Extracts, reviews, and original contributions became

plentiful; our weeklies, monthlies, and quarterlies contained much that was and much that still is of value. The first extensive American papers on diphtheria (1860) and acute rheumatism (1875) were published in magazines. The first volumes of the *American Journal of Obstetrics and the Diseases of Women and Children* (founded in 1869) were almost entirely filled with subjects connected with the anatomy, physiology, and therapeutics of the young. But though the Germans had a special journal since 1843, the first American journal, the *Archives of Pediatrics*, was published by the enthusiastic Watson in 1884 and *Pediatrics* by Dillon Brown in 1896. My readers know that both have rendered good service, both by disseminating knowledge and rousing interest and enthusiasm. At the same time our weeklies have vied with them in supplying the practitioners of the country with information of increasing value.

What all of us have learned is to look on pediatrics not as a specialty, such as ophthalmology or otology, which concern single organs, but as that part of internal medicine and surgery which cannot be measured by the knowledge derived from and applied to the adult; it requires special study and research in order to become both scientific and practical. We learned that there is no uniformity of structure and function in the human organism between conception and death; that childhood must be studied, not from the point of view of reproduction only, but of reproduction *and growth*; that pediatrics does not deal with miniature men and women, with reduced doses and the same class of diseases in smaller bodies, but has its own independent range and horizon, and gives as much to general medicine as it has received from it; that there are anomalies and diseases which are encountered in the infant and child only. On the other hand, there are those which are *mostly* found in children, or with a symptomatology and course peculiar to them; and those, finally, which affect both the young and the old, with such varieties, however, in both symptoms and course, as depend on the size or anatomic structure of the afflicted organ or organism, or the difference in the degree of irritability.¹

To learn and to teach all that—and many more things—the cooperation of many interests was required. The general practitioner—the majority of whose patients are young—since the belief ceased to be prevalent that the diseases of the small child are “small things,” wanted more opportunities to learn than those which his college schooling had pro-

1. Arch. Pediat., November, 1889.

vided for him. The colleges themselves have not been slow in recognizing the advanced condition of pediatrics and the necessities of the physicians of the country.

The increased number of medical magazines—suggested by medical men and published by business men eager to profit by subscriptions and by ethical and unethical advertisements—and text-books—a few excellent, some good, many more, however, mere compilations, most of them with ample sales—have disseminated knowledge which without them would not have been accessible. Even inferior books will convey it and render their owners amenable to the consciousness of their defects and the longing for something more that is not only new but better. For, indeed, the latest is not necessarily the best.

The number of special journals dedicated to pedology or to pediatrics has become quite large. Germany began its oldest and most exclusive "*Journal für Kinderkrankheiten*," in 1843; it has six or seven such magazines at present; another one appeared lately on account of the large amount of material offered, swamping those in existence. France, England, Spain, Italy, Turkey, and America, all have their special journals. Meanwhile the large weeklies and monthlies have continued to contribute information to those who are interested in pediatrics. In Germany, however, where special pediatric magazines are most numerous and widely appreciated, the pediatric contributions to general journals are becoming less predominant.

The same process of spontaneous exclusiveness will keep on when pediatric journals are published in sufficient numbers and of such a character as to justify and tempt authors to select them for their contributions. But journals are not all of the same standard. Mere compilations will find many grateful readers; a single interesting case accompanied by intelligent culling will prove as acceptable to many a subscriber as it is pleasing to the eye of the writer; discussions in medical societies will frequently add more to the knowledge of a given subject than a labored article on a topic studied up for the instruction, at least, of the author; extracts from the current literature of all nations, particularly when full and systematized, are eagerly sought for and enjoyed.

This new journal of ours, the AMERICAN JOURNAL OF DISEASES OF CHILDREN, however, the first number of which we herewith offer to the profession, is not published to compete with those already in existence.

For some time it has been noted, however, that the pediatric material offered to *The Journal of the American Medical Association* is rapidly increasing in quantity, and also in the size of the articles. Writers were often annoyed by the delay encountered in the publication of their essays; it has even happened that after a delay of many months, authors of the very highest standing were requested to shorten their articles—in many instances an impossible task. Such occurrences suggested the publication of a new special organ. Even those who insisted on the right of the practitioners of the country—members of the Association—to be amply supplied with pediatric teaching by their own journal, receded from the stand taken by them when convinced by the fact that a new journal would not curtail the printing of pediatric contributions in *The Journal of the American Medical Association* and many others of high standing. On the contrary, with the increasing number of physicians interested and working in the field of pedology, there will be more than merely a vast number of papers; there will be more profundity and research. These our new journal is to gather in, and it is to be the companion and ally of the *Archives of Internal Medicine*. It may rarely give a mere case, still more rarely a prescription; it is to be a receptacle, however, of the very latest in the very best of American and European literatures. But extracts will be few in proportion. Reviews, carefully prepared by competent critics, will be offered from time to time. The bulk of the contents, however, will be original; anatomy—both embryonal and postnatal—physiology, biochemistry, nosology, and therapeutics will come to their own, and will be welcomed as our sources of actual progress. Thus, THE AMERICAN JOURNAL OF DISEASES OF CHILDREN is expected to be one of the number of strictly scientific magazines which, since the first appearance of the *Journal of Experimental Medicine* and its followers, have given American medical journalism its standing as an equal coworker in the modern world of Medicine. *Quod felix faustumque sit.*

A. JACOBI.

SOME ANATOMIC FEATURES OF THE CHILD'S THORAX AND THEIR PRACTICAL APPLICATION IN PHYSICAL DIAGNOSIS *

GEORGE FETTEROLF, M.D. AND J. CLAXTON GITTINGS, M.D.

PHILADELPHIA

Since the study of anatomy by means of frozen sections and the use for the same purpose of bodies with the viscera hardened *in situ* have come into vogue, many new ideas have been acquired and many misconceptions corrected. While the study of soft preparations in the dissecting and autopsy rooms has been responsible for almost all our knowledge of gross anatomy, it is not until we examine conditions more nearly as they are during life that we get a really true conception of anatomic relations. The mere opening of the thorax and abdomen under ordinary conditions will of itself cause a change in the shape and relations of the various organs, and when conditions are still further disturbed by dissection or by the successive stages of an autopsy it is possible to get only an approximate idea of conditions as they existed during life.

Our work has consisted of making dissections and of cutting sections of the bodies of infants which had been injected with 10 per cent. dilution of liquor formaldehydi and then frozen. The results of our study of these preparations are embodied in the present paper.

Examination of the child's thorax reveals many important facts, the conception of which is generally inexact. One of these facts is that the thymus body is a structure of considerable size and extent, reaching well beyond the borders of the sternum and separating widely the upper lobes of the two lungs (Figs. 1, 3 and 4). Posteriorly, at least in the first few weeks of life, it extends in places to the trachea (Figs. 2 and 6). It would seem that sudden death at this period, due to respiratory failure, might be caused by even moderate increase in the size of the gland. Delay in the normal involution of this body would extend the danger period.

A point which is very noticeable in the hardened gland is that the upper median portion is deeply indented posteriorly (Fig. 5) by the left innominate vein, which lies immediately on the anterior facies of the

* From the Laboratory of Anatomy of the University of Pennsylvania.

* Read before the joint meeting of the Pediatric Section of the New York Academy of Medicine and the Philadelphia Pediatric Society, Philadelphia, Nov. 8, 1910.

trachea (Fig. 6). When the size and distensibility of this vessel and the softness and small caliber of the trachea are taken into consideration we have a possible mechanical explanation of the sudden deaths which occur in the young during anesthesia. A slight embarrassment of the right heart or any factor, such as struggling, which would cause a rise of venous pressure, would dilate this vein. Braced firmly on its anterior surface by the thymus, the only direction in which it could extend would be posteriorly and in such an event there would be of necessity compression to a greater or less extent of the trachea. If the amount of compression were great, sudden death would be the result. If of a slighter degree the amount of asphyxia caused by it would tend to raise pressure and cause still further dilatation of the innominate vein, and thus a vicious circle would be established which would soon result in death. If there is any truth in this theory, venesection would be indicated in the emergency.

Another noteworthy point is the amount of space occupied by the heart, which extends at its greatest depth from the sternum to the esophagus, aorta and spinal column (Figs. 7, 8 and 9). In this connection it is evident that a dilated heart or pericardium must exert such marked pressure on the lower third of the upper lobe and the upper two-thirds of the lower lobe of the left lung (Figs. 7 and 8), that in such conditions the frequent presence of bronchial breathing, heard over the back of the chest, is easily accounted for.

It is a well-known fact that in infancy the ribs lie nearly in a horizontal plane and that the sternum occupies a higher position than in the adult, its top lying opposite the body of the first thoracic vertebra.¹ Later in life the sternum drops to a lower plane, owing probably to increase in the size of the lungs, a relative decrease in size of the liver, an actual decrease in size of the thymus and the assumption by the child of the vertical as opposed to the horizontal position.

The internal anatomy of the heart shows many points of interest.

The right auricle lies directly in front of the right half of the left auricle (Fig. 10) but, with the exception of a portion of the appendix (Fig. 9), does not touch the chest wall. The superior vena cava enters the auricle in a plane anterior to that of the inferior cava (Fig. 11). Blood from the latter is directed upward by the Eustachian valve and not to the left, as is commonly supposed. The foramen ovale lies in an almost horizontal plane (Fig. 11), and not vertically and facing to the left. Dextro- or levo-position of the new-born is, therefore, of no importance in aiding the closure of this opening, a point to be elaborated in a future communication.

The tricuspid orifice, an oval ring, is practically vertical (Fig. 12), not horizontal, and opens to the left and slightly forward. The bottom

1. Piersol, George A.: *Human Anatomy*, 1907, p. 164.

of the right ventricle is so nearly on the level of that of the right auricle (Fig. 12) that gravity must play little if any part in the passing of the blood through the tricuspid orifice. The negative pressure caused by the ventricular diastole and the veno-auricular pressure are the principal factors favoring the rapid filling of the ventricle.

The right ventricle constitutes practically all of the heart which touches the anterior chest wall (Figs. 7 and 12) and is slightly overlapped on each side by the right and left lungs (Fig. 7). Posteriorly it is bounded by two structures, the left ventricle below (Figs. 7 and 15) and the root of the aorta above (Fig. 12). Aortic sounds, therefore, at the level of the second costal cartilage must be heard through the medium of the upper part of the right ventricle, that part known as the infundibulum or conus arteriosus (Figs. 8 and 12), from which arises the pulmonary artery.

The pulmonary artery lies to the left of and slightly anterior to the aorta (Fig. 4) and is separated from the anterior chest wall by the lower portion of the thymus body (Fig. 4). It divides into a long right branch and a short left one. The former runs under the aortic arch and continues along the upper border of the left auricle (Figs. 9 and 12). The left branch passes to the root of the lung across and directly in front of the left bronchus (Fig. 4).

The left auricle is a horizontal cylinder flattened from before backward (Figs. 9 and 12), lying at the extreme back of the heart and extending throughout the entire width of the base of the heart (Fig. 10). It is bounded in front by the right auricle and the left ventricle (Fig. 10), behind by the thoracic aorta (Figs. 9 and 10) and esophagus (Fig. 10), and above by the right pulmonary artery and the left bronchus (Figs. 9 and 12). The right end lies directly behind the right auricle (Fig. 10) and consists of the orifices of the two right pulmonary veins (Fig. 9). At the left end are four openings (Fig. 12). Above and posteriorly are those of the two left pulmonary veins, while above and anteriorly is the opening of the auricular appendix, the two being separated by a practically vertical septum. Below and anterior is the fourth opening, the mitral orifice, which lies in a plane approximately parallel to the anterior facies of the vertebral column (Fig. 12) at this level. The mitral and tricuspid orifices, therefore, lie in planes which are almost at right angles to each other (Fig. 12).

The left ventricle is bounded behind by the left auricle (Fig. 7), and in front, except for the extreme left hand edge, by the right ventricle (Figs. 7 and 13). The two posterior leaflets of the aortic valve are attached to the base of the anterior mitral leaflet (Fig. 12), a fact which furnishes the most plausible theory to account for the mechanism of a "Flint's murmur."

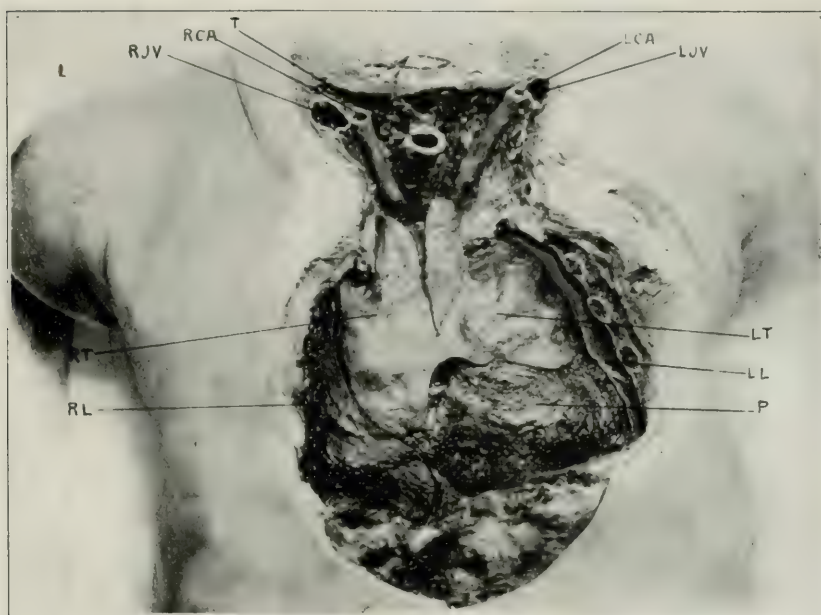


Fig. 1.—Body of a new-born child from which the median portion of the anterior chest wall has been removed. RL, right lung; RT, right lobe of thymus; RJV, right internal jugular vein; RCA, right common carotid artery; T, trachea; LCA, left common carotid artery; LJV, left internal jugular vein; LT, left lobe of thymus; LL, left lung; P, pericardium.

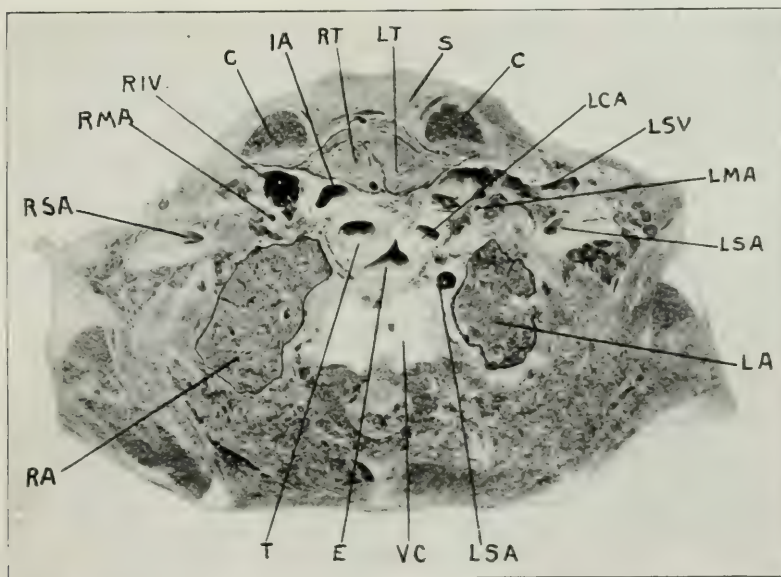


Fig. 2.—Horizontal section, viewed from below of the body of a new-born child at the level of the upper part of the sterno-clavicular articulation. VC, vertebral column; E, esophagus; T, trachea; RA, apex of right lung; RSA, right subclavian artery; RMA, right internal mammary artery; RIV, right innominate vein; C, C, clavicles; IA, innominate artery; RT, right lobe of thymus; LT, left lobe of thymus; S, sternum; LCA, left common carotid artery; LSV, left subclavian vein; LMA, left internal mammary artery; LSA, LSA, left subclavian artery; LA, apex of left lung.

The arch of the aorta passes almost directly backward (Figs. 4, 9 and 12), instead of from right to left. When it is recognized that the aorta arises from the heart to the left of the midsternal line and descends in the thorax, but slightly to the left of the middle of the vertebral column, this position of the arch is readily understood. In its course backward and very slightly to the left it separates the lower part of the trachea from the adjacent portion of the left lung (Fig. 3), making a distinct arciform groove in the mediastinal facies of the latter organ.

When the heart is considered *in toto* it is seen that the only portions which touch the anterior chest wall are a part of the right auricular

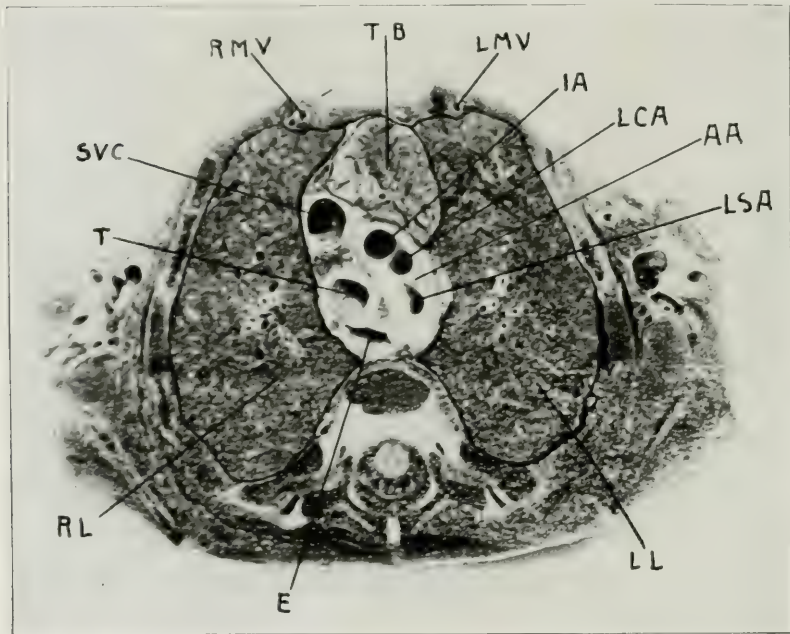


Fig. 3. Horizontal section, viewed from below, of the body of a new-born child at the level of the upper border of the second rib. E, esophagus; RL, right lung; T, trachea; SVC, superior vena cava; RMV, right internal mammary vessels; TB, thymus body; LMV, left internal mammary vessels; IA, innominate artery; LCA, left common carotid artery; AA, aortic arch; LSA, left subclavian artery; LL, left lung.

appendix and all of the right ventricle, except perhaps the upper part of the infundibulum. The tip of the left ventricle, while it may come into contact with the chest wall, is probably covered by the tip of the lower lobe of the left lung (Fig. 7), that part called the lingula.

Examination of the position of the greater azygos vein (Fig. 11) makes clear the fact that pressure on it by a dilated heart is impossible,

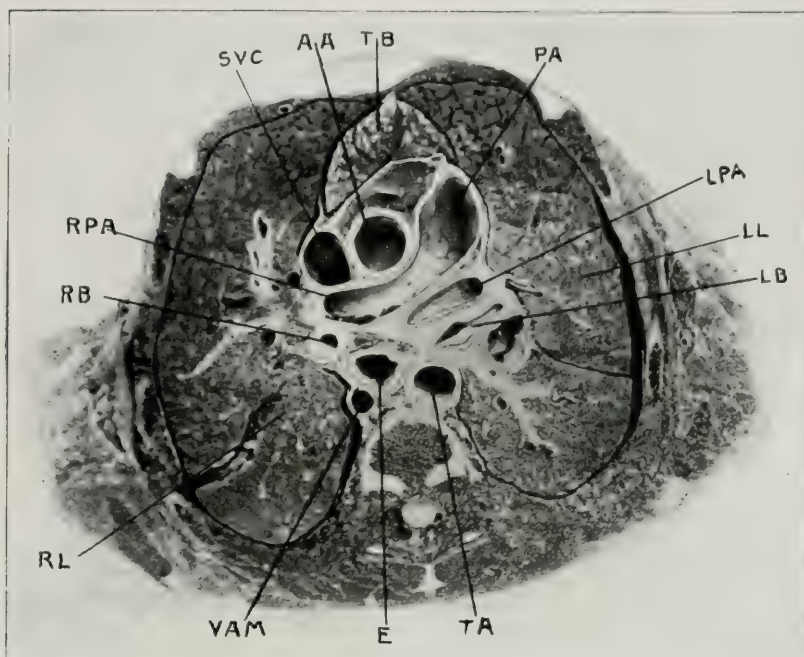


Fig. 4.—Horizontal section, viewed from below, of the body of a new-born child at the level of the upper border of the third rib. E, esophagus; VAM, vena azygos major; RL, right lung; RB, right bronchus; RPA, right pulmonary artery; SVC, superior vena cava; AA, ascending part of aortic arch; TB, thymus body; PA, pulmonary aorta; LPA, left pulmonary artery; LL, left lung; LB, left bronchus; TA, thoracic aorta.

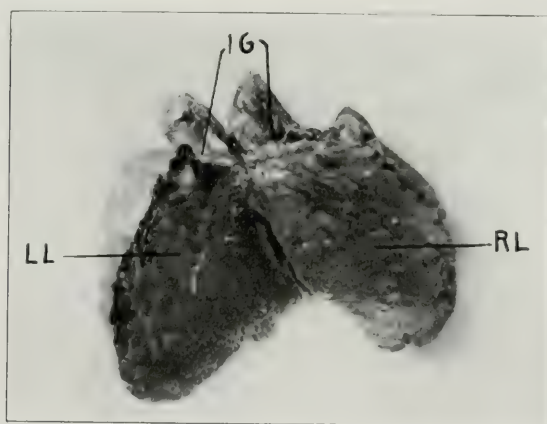


Fig. 5.—Posterior view, life size, of the thymus body of the new-born child depicted in Figs. 1 and 6. LL, left lobe; IG, groove for left innominate vein; RL, right lobe.

whereas pressure on the pulmonary veins, especially the right, can occur with even moderate degrees of cardiac enlargement (Fig. 17). Partial occlusion of these latter veins would explain in large part both the hydrothorax and the pulmonary congestion which are seen in many cases of enlarged heart without signs of stasis in the systemic circuit.

If, in the case of mitral regurgitation, the problem were simply one of overcoming the leakage by the force necessary to pump through the pulmonary artery the normal amount of venous blood, plus the arterial blood, which is returned from the left auricle, the right ventricle would probably be efficient for a long time. From the beginning of mitral leakage, how-

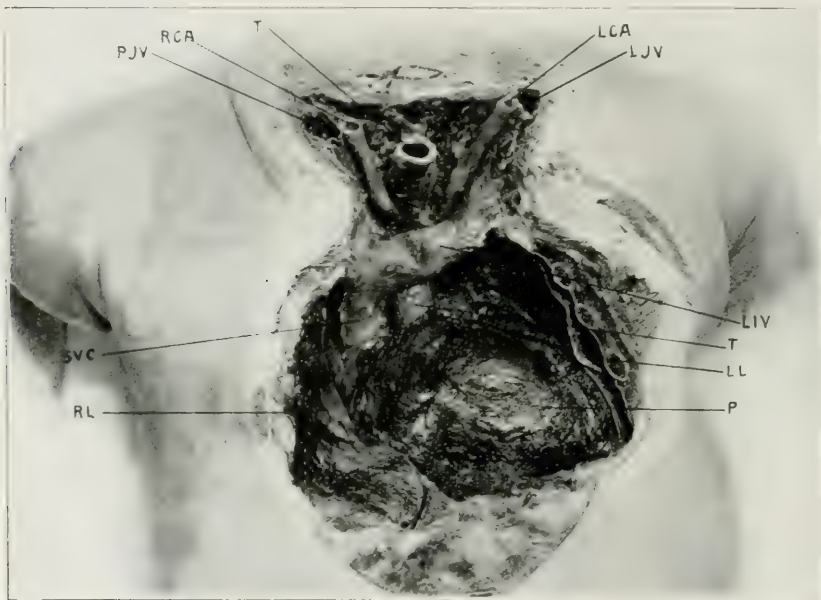


Fig. 6.—Body of the new-born child depicted in Fig. 1, the thymus having been removed. RL, right lung; SVC, superior vena cava; RJV, right internal jugular vein; RCA, right common carotid artery; T, T, trachea; LCA, left common carotid artery; LJV, left internal jugular vein; LIV, left innominate vein; LL, left lung; P, pericardium.

ever, two changes take place, enlargement of the left auricle and, although not quite as early, a similar change in the left ventricle. The former must include enlargement of the appendix as well as of the main cavity, and the appendix, if at all increased in size, is sure to exert pressure on the upper left pulmonary vein, while enlargement of the ventricle would cause pressure on the lower vein (Fig. 18). Compression of these veins at once favors congestion in the radicles, both arterial and venous, in the lung and pleura, the veins of the human pleura opening as they do into

the pulmonary veins,² so that the right ventricle has to overcome both this congestion and the back flow which takes place during systole of the left ventricle. In the same manner enlargement of the right auricle causes pressure on the right pulmonary veins (Fig. 17), and it seems to us highly probable that it is this factor of pressure on the pulmonary veins³ which aids materially in producing pulmonary congestion and pleural leakage, as well as in promoting failure of competence of the right side of the heart.

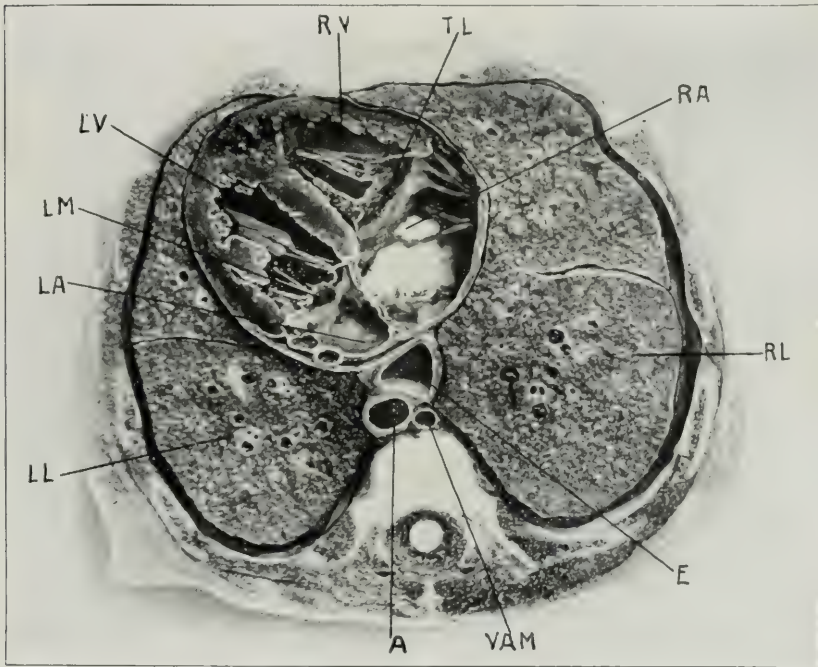


Fig. 7.—Horizontal section, viewed from above, of the body of a new-born child at the level of the upper border of the fifth rib. A, thoracic aorta; LL, left lung; LA, left auricle; LM, mitral leaflet; LV, left ventricle; RV, right ventricle; TL, tricuspid leaflet; RA, right auricle; RL, right lung; E, esophagus; VAM, vena azygos major.

The relatively loud sound of the closure of the pulmonary valve in children, as compared with that of the aortic, may be due in part to the fact that the upper lobe of the left lung does not cover the pulmonary artery (Fig. 16) as well as in adults and possibly to the presence of the thymus (Fig. 16), which would furnish a good conducting medium from

2. Miller, W. S.: *Am. Jour. Anat.*, vii, 404, 405.

3. Fetterolf and Landis: *Am. Jour. Med. Sc.*, November, 1909.

valve to chest wall. More important, however, is the physiologic difference in systemic tension between child and adult.

From a correct conception of the position of the heart *in vivo* we may draw conclusions as to the pathologic anatomy in case of enlargement. Increase in size to the left would be due mainly to enlargement of the left ventricle (Fig. 7); to the left and upward mainly to the left auricular appendix (Fig. 18) and to a slight extent the left auricle (Fig. 10); to the left and downward to the left and right ventricles (Figs. 7 and 13). Enlargement to the right would involve mainly the right auricle

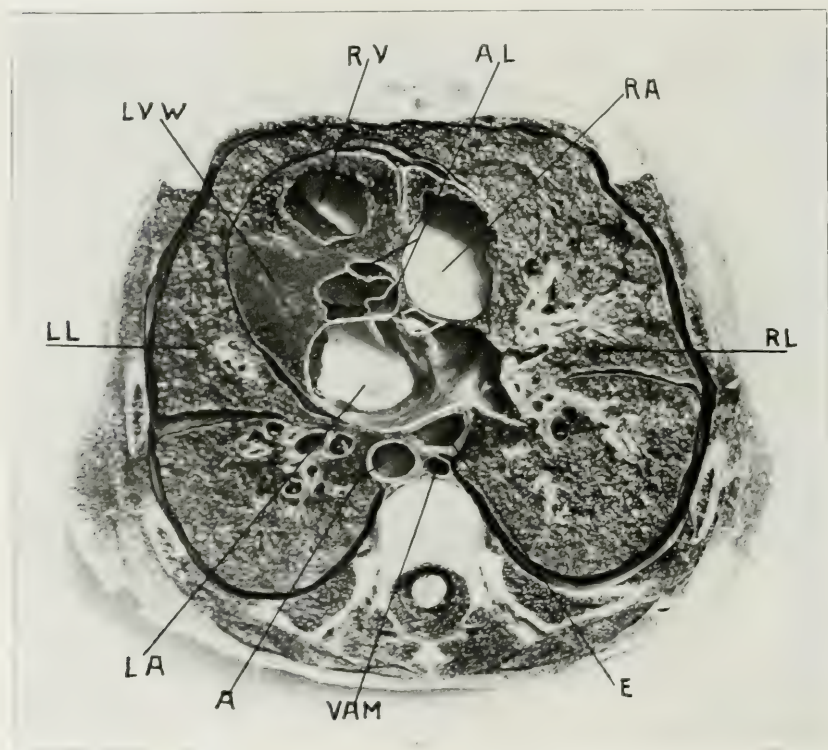


Fig. 8.—Horizontal section, viewed from above, of the body of a new-born child at the level of the upper border of the fourth rib. VAM, vena azygos major; A, aorta; LA, left auricle; LL, left lung; LVW, left ventricular wall; RV, right ventricle; AL, aortic leaflet; RA, right auricle; RL, right lung; E, esophagus.

and appendix (Fig. 11), and to a lesser extent the right ventricle and the right end of the left auricle (Fig. 11).

A noteworthy point is that the mitral, tricuspid and aortic valves are practically contiguous structures (Fig. 12). This readily explains the difficulty in distinguishing the murmurs produced in cases of double or

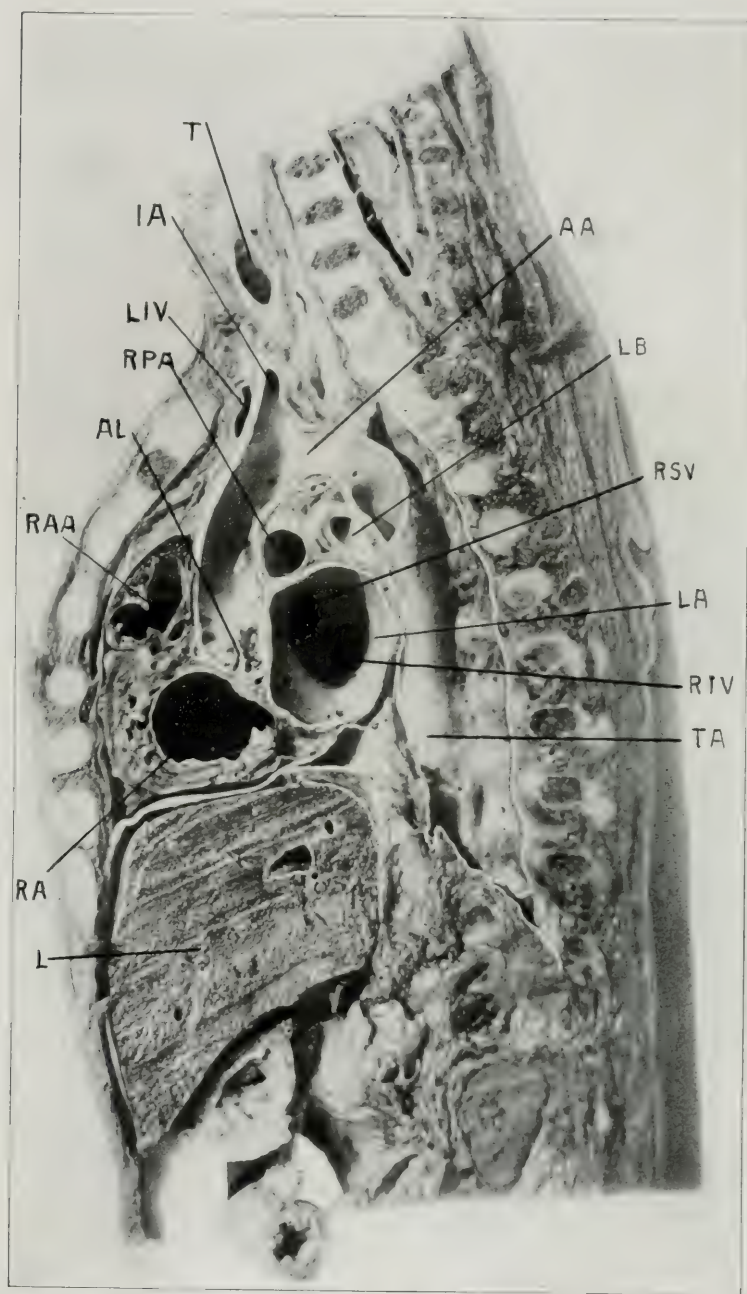


Fig. 9.—Sagittal section, viewed from the left, of the body of a new-born child, the plane of section being 0.75 cm. to the left of the midsternal line. L, liver; RA, right auricle; RAA, right auricular appendix; AL, aortic leaflets; RPA, right pulmonary artery; LIV, left innominate vein; IA, innominate artery; T, trachea; AA, aortic arch; LB, left bronchus; RSV, right superior pulmonary vein; LA, left auricle; RIV, right inferior pulmonary vein; TA, thoracic aorta.

triple lesions or leakage. When we add to this the ease with which cardiac sounds, both normal and abnormal, can be heard in children, owing principally to the thinness of the chest wall, it would appear that a differentiation between a mitral and a tricuspid regurgitation, for example, would be impossible from the murmurs alone. A systolic murmur heard in the left axilla but not in the carotids or right axilla, would indicate mitral regurgitation. An aortic systolic murmur can be diagnosed with certainty only in the neck, while a systolic murmur heard over the heart, but not in the left axilla or in the neck, would point more strongly to a

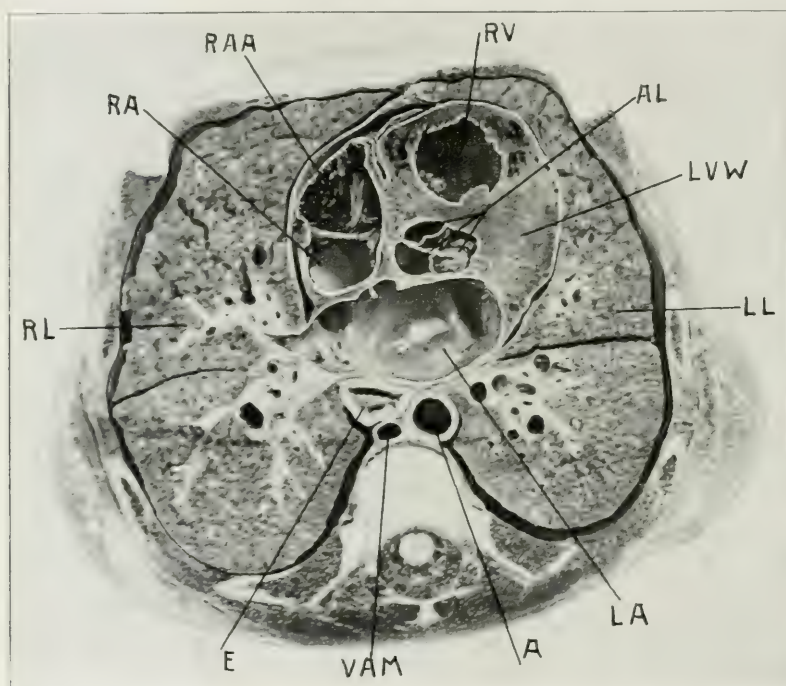


Fig. 10. -Horizontal section, viewed from below, of the body of a new-born child at the level of the upper border of the fourth rib. VAM, vena azygos major; E, esophagus; RL, right lung; RA, right auricle; RAA, right auricular appendix; RV, right ventricle; AL, aortic leaflets; LVW, left ventricular wall; LL, left lung; LA, left auricle; A, aorta.

functional cause than to tricuspid regurgitation. A pure diastolic murmur heard anywhere over the heart is usually due to aortic regurgitation.

Some interesting features in regard to the lungs have been noted. Everyone is familiar with the normal relative differences between the physical signs over the right and left apices. Various explanations have

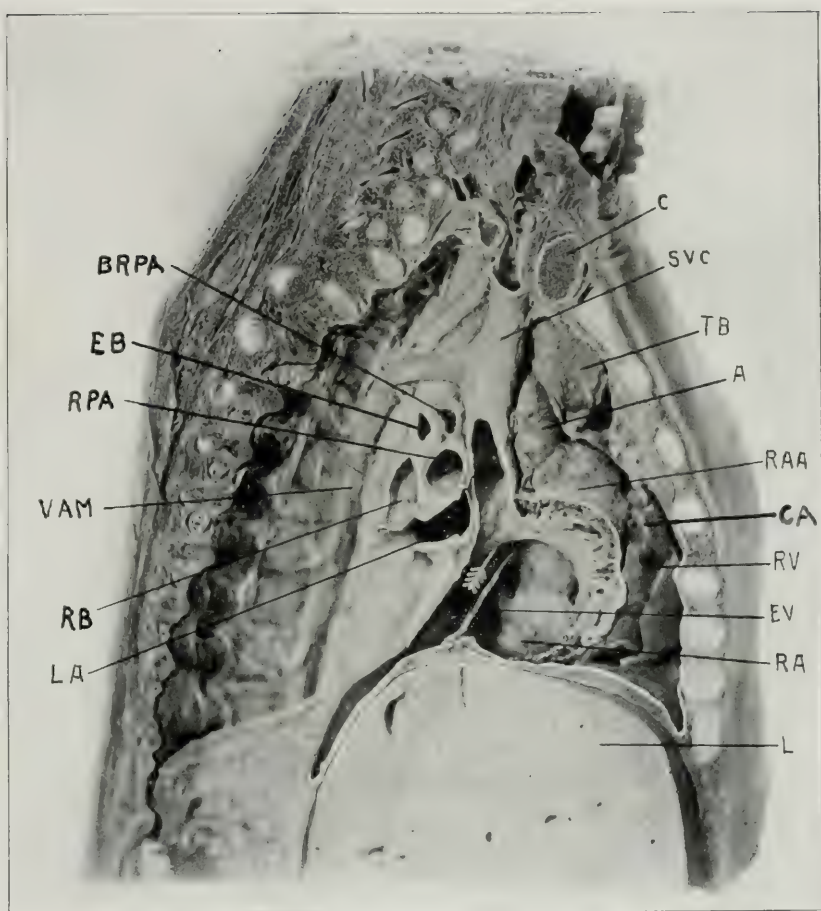


Fig. 11.—Sagittal section, viewed from the right, of the body of a new-born child, the plane of section being 0.75 cm. to the right of the midsternal line. LA, left auricle; RB, right bronchus; VAM, vena azygos major; RPA, right pulmonary artery; EB, eparterial bronchus; BRPA, branch of right pulmonary artery; C, clavicle; SVC, superior vena cava; TB, thymus body; A, root of aorta; RAA, right auricular appendix; CA, conus arteriosus; RV, right ventricle; EV, Eustachian valve; RA, right auricle; L, liver. The arrow is in the foramen ovale.

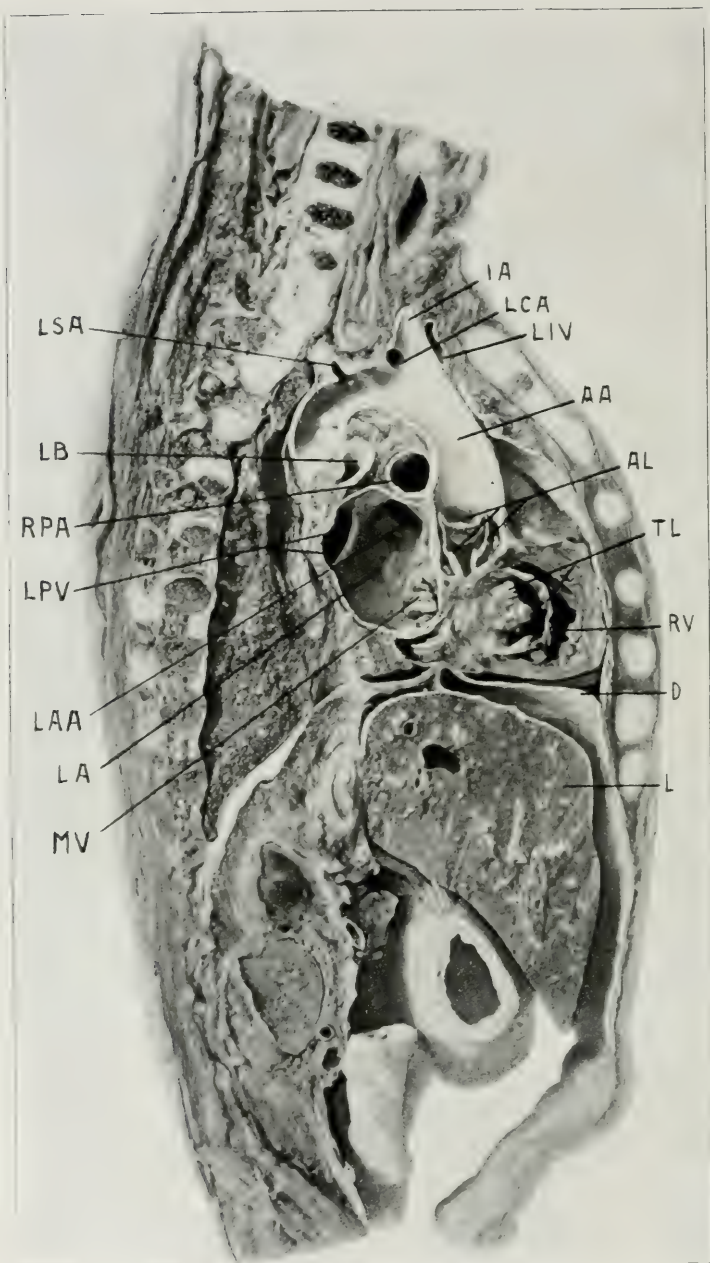


Fig. 12.—Sagittal section, viewed from the right, of the body of a new-born child, the plane of section being 0.75 cm. to the left of the midsternal line. MV, mitral valve; LA, left auricle; LAA, left auricular appendix; LPV, orifices of left pulmonary veins; RPA, right pulmonary artery; LB, left bronchus; LSA, left subclavian artery; IA, innominate artery; LCA, left common carotid artery; LIV, left innominate vein; AA, aortic arch; AL, aortic leaflets; TL, tricuspid leaflets; RV, right ventricle; D, diaphragm; L, liver.

been offered from time to time but the one pointed out by one of us⁴ is shown clearly in our preparations. This explanation rests on the anatomic relations of the trachea and the pulmonary apices. On the right side they are absolutely contiguous structures (Fig. 2), while on the left they are separated by the aorta, the left carotid and subclavian arteries, the esophagus and some areolar and lymphoid tissue (Fig. 2). In this connection should be mentioned the dulness to the left of the upper sternum to which attention has been called by Hamill and LeBoutillier.⁵ This is probably due partly to the facts just mentioned, partly to the exposure of

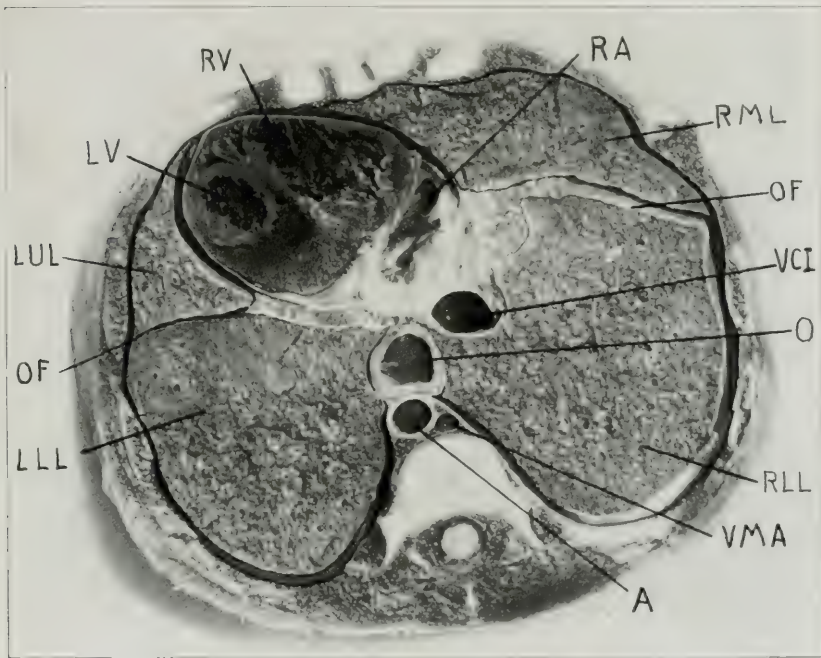


Fig. 13.—Horizontal section, viewed from above, of the body of a new-born child at the level of the upper portion of the ensiform cartilage. LLL, lower lobe of left lung; OF, oblique fissure of left and right lungs; LUL, upper lobe of left lung; LV, left ventricle; RV, right ventricle; RA, right auricle; RML, middle lobe of right lung; VCI, vena cava inferior; O, esophagus; RLL, lower lobe of right lung; VMA, vena azygos major; A, aorta.

the pulmonary artery on account of the posterior position of the anterior margin of the left lung as compared with the adult, and partly to the

4. Fetterolf, George: The Anatomic Explanation of the Greater Amount of Vocal Fremitus and Vocal Resonance Normally Found at the Apex of the Right Lung, *Arch. Int. Med.*, February, 1909, p. 23.

5. Hamill, Samuel McC., and LeBoutillier, Theodore: Some Physical Signs in Infants and Children Not Sufficiently Emphasized, *Jour. Am. Med. Assn.*, Jan. 7, 1905, p. 26.

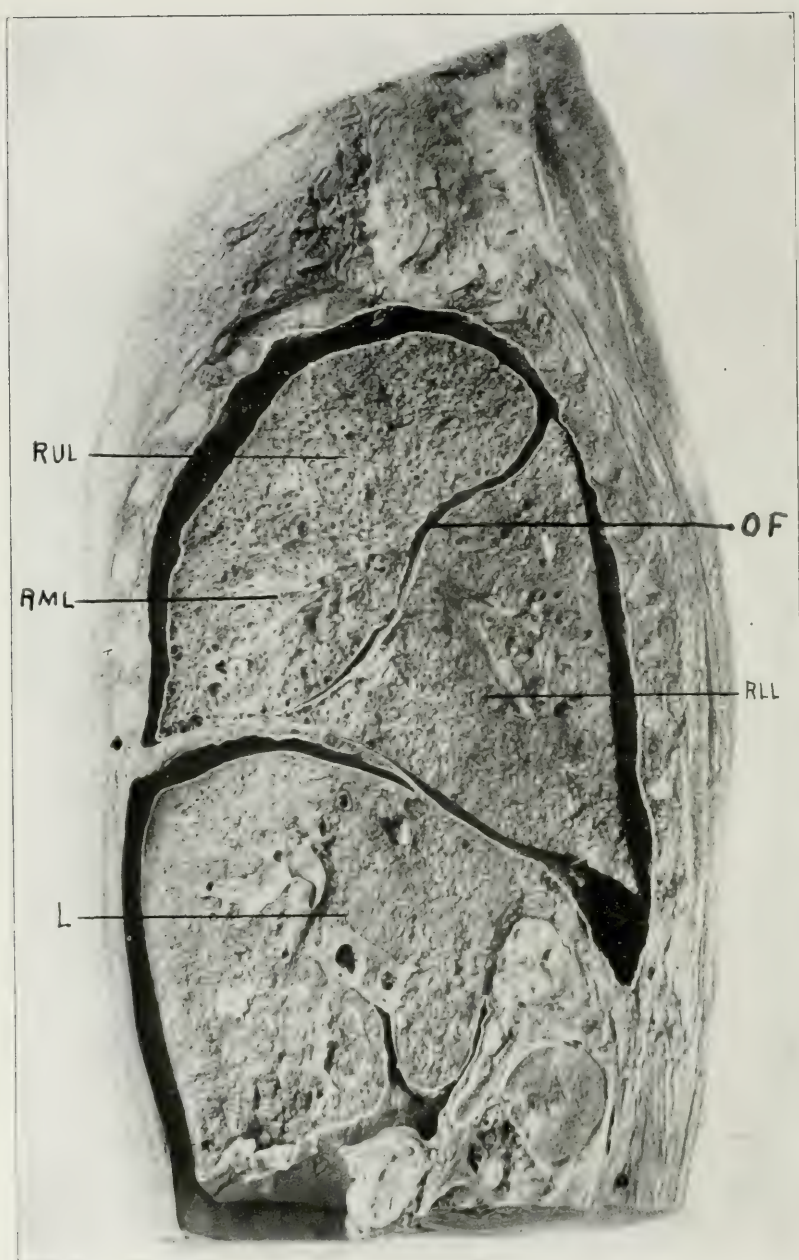


Fig. 14.—Sagittal section, viewed from the left, of the body of a new-born child, the plane of section being 2 cm. to the right of the midsternal line. Owing to adhesions the horizontal fissure is not shown. L, liver; RML, middle lobe of right lung; RUL, upper lobe of right lung; OF, oblique fissure; RLL, lower lobe of right lung.

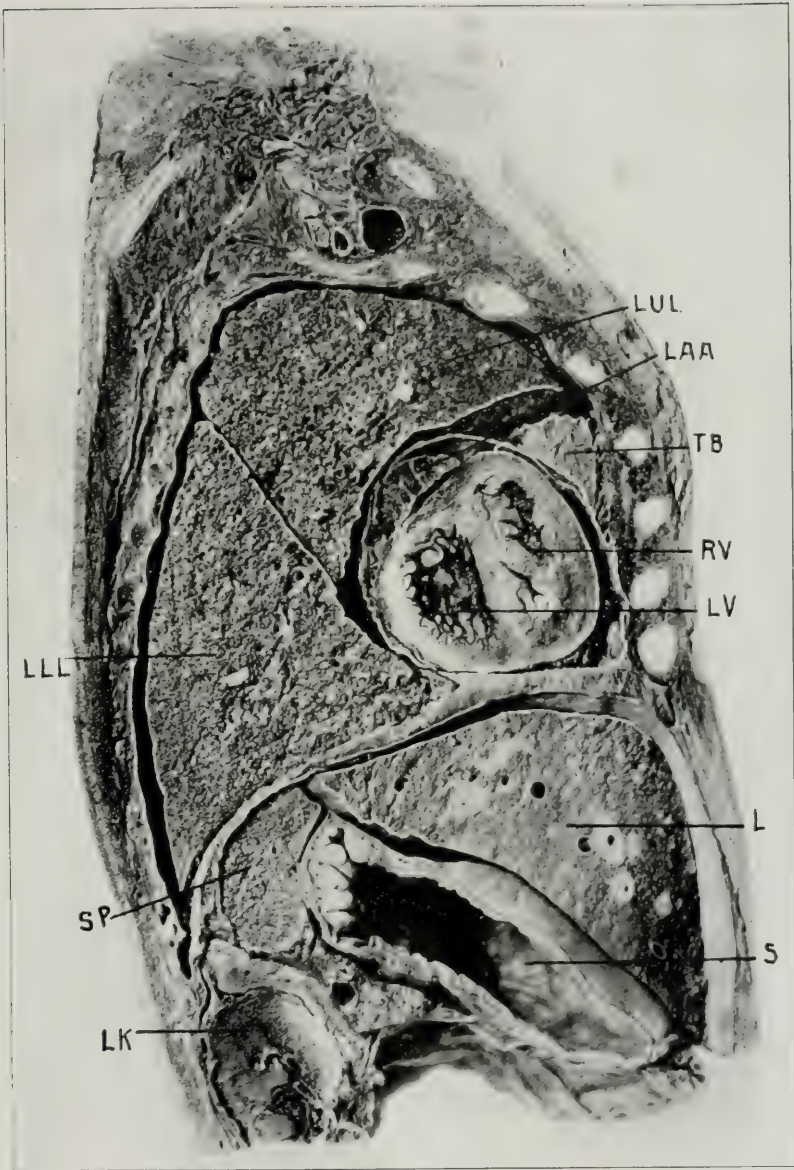


Fig. 15.—Sagittal section, viewed from the right, of the body of a new-born child, the plane of section being 2 cm. to the left of the midsternal line. LK, left kidney; SP, spleen; LLL, lower lobe of left lung; LUL, upper lobe of left lung; LAA, left auricular appendix; TB, thymus body; RV, right ventricle; LV, left ventricle; L, liver; S, stomach.

greater extent of the left lobe of the thymus (Fig. 1). In addition, the left lobe of the thymus is backed by a mass of solid tissue interposed between the left upper lobe and the trachea, while the right lobe is backed by resonating tissue in the shape of the right upper pulmonary lobe.

The high position of the dome of the liver on the right side is clearly demonstrated (Figs. 11 and 14) and explains the high-pitched or relatively dull note which is heard in percussing over the right pulmonary base. On the left side the spleen is seen to reach a level almost as high as that of the liver, the difference being not more than that of a rib and interspace.

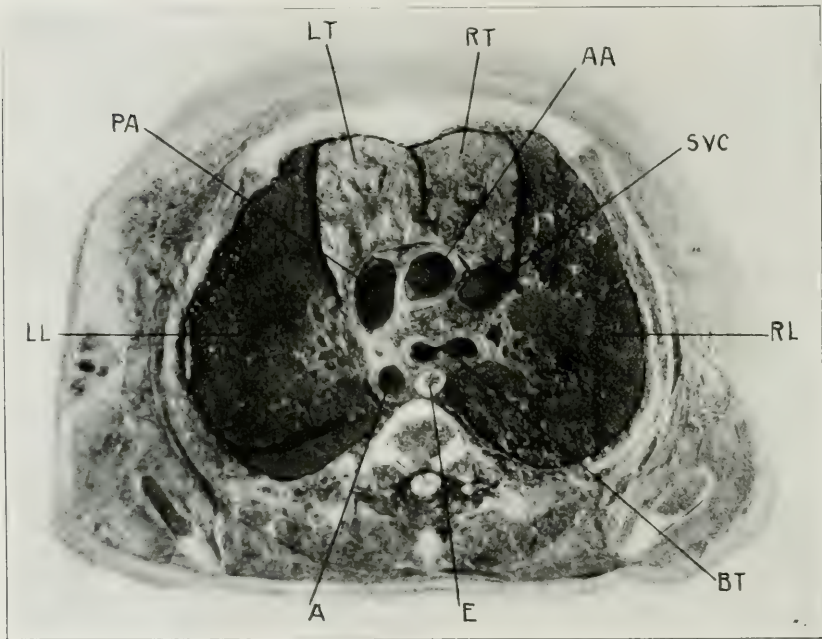


Fig. 16.—Horizontal section, viewed from above, of the body of a new-born child at the level of the upper border of the third rib. LL, left lung; PA, pulmonary aorta; LT, left lobe and RT, right lobe of thymus body; AA, ascending part of aortic arch; SVC, superior vena cava; RL, right lung; BT, bifurcation of trachea; E, esophagus; A, descending part of aortic arch.

The edge of the lung which overlaps the right border of the heart is so thin (Fig. 10) that it should hardly interfere with a reasonably accurate determination of the right border of cardiac dulness.

The position of the bronchial lymph nodes at the bifurcation of the trachea (Fig. 16) is so far above the heart, which would furnish a conducting medium, that it is difficult to conceive how enlargement of these nodes could produce a bruit, even on forced extension of the head, which

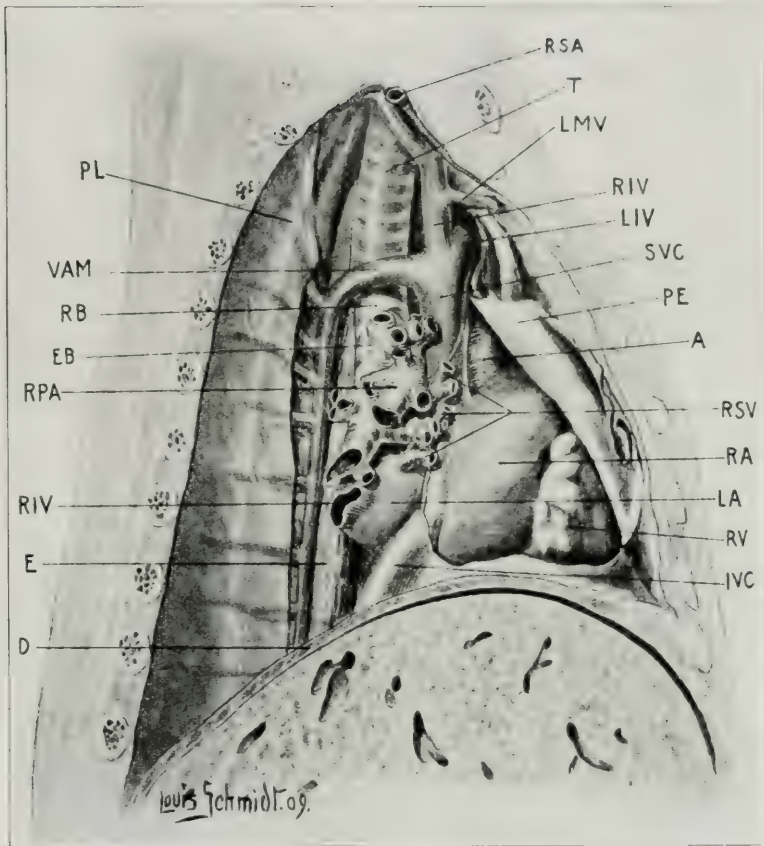


Fig. 17.—View from the right of the mediastinal contents and the root of the lung of the body of a 6-months-old child. D, diaphragm; E, esophagus; RIV, right inferior pulmonary vein; RPA, right pulmonary artery; EB, eparterial bronchus; RB, right bronchus; VAM, vena azygos major; PL, pleura; RSA, right subclavian artery; T, trachea; LMV, right internal mammary vein; RIV, right innominate vein; LIV, left innominate vein; SVC, superior vena cava; PE, pericardium; A, aorta; RSV, right superior pulmonary vein; RA, right auricle; LA, left auricle; RV, right ventricle; IVC, inferior vena cava. (Fetterolf and Landis: *Am. Jour. Med. Sc.*, November, 1909.)

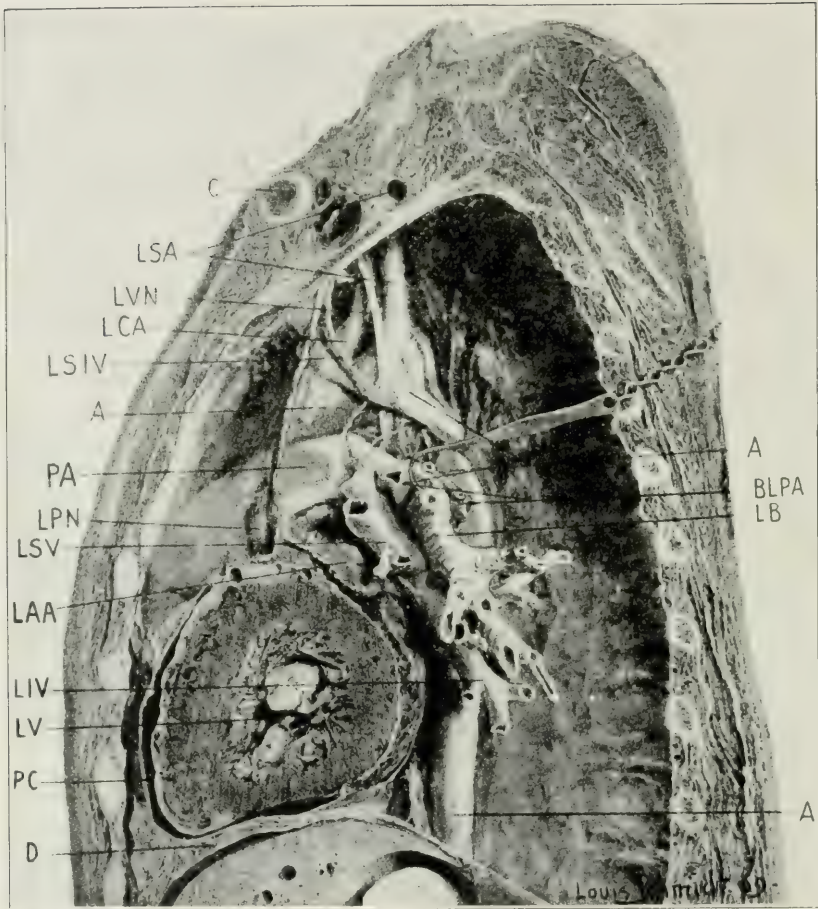


Fig. 18.—View from the left of the mediastinal contents and root of the left lung of the body of an adult. D, diaphragm; PC, pericardial chamber; LV, left ventricle; LIV, left inferior pulmonary vein; LAA, left auricular appendix; LSV, left superior pulmonary vein; LPN, left phrenic nerve; PA, pulmonary artery; A, aorta; LSIV, left superior intercostal vein; LCA, left common carotid artery; LVN, left vagus nerve; LSA, left subclavian artery; C, clavicle; A, A, A, aorta; BLPA, branch of left pulmonary artery; LB, left bronchus. (Fetterolf and Landis: *Am. Jour. Med. Sc.*, November, 1909.) This section, while that of an adult, shows the points under discussion so well that it is used in preference to preparing a new dissection of an infant.

could be heard over the upper sternum. The explanation of this bruit would seem to depend rather on the persistence of the thymus, which could exert pressure on the vessels as they arise from the arch of the aorta (Fig. 3).

Since the bronchial nodes are surrounded by so many other structures which would give a dull note on percussion, such as the arch of the aorta, the great vessels, and the thymus, it seems to us highly problematical that enlargement of these nodes can be accurately diagnosed by percussion.

Finally, the sections afford a clear demonstration of the position of the lobes of the lungs and emphasize the fact that physical signs in the lungs posteriorly, as high as the base of the spines of the scapulæ, are produced in the lower lobes (Figs. 14 and 15). Anteriorly, on the right, the fourth rib divides the upper from the middle lobe, while on the left any signs heard above the heart and in front of the anterior axillary line would denote that the upper lobe is affected.

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OBSERVATIONS ON THREE HUNDRED CASES OF ACUTE MENINGITIS IN INFANTS AND YOUNG CHILDREN

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NEW YORK

With the introduction of lumbar puncture the diagnosis of acute meningitis entered on a new phase. This is quite as important an advance in this group of diseases as was the adoption of throat cultures in diphtheria and other throat affections. Exact diagnosis has now become possible where formerly in very many cases only a probable diagnosis could be made. The period during which lumbar puncture has been systematically performed on all suspected cases in the Babies' Hospital covers the last five years.

The observations included in this paper relate to 300 cases of acute meningitis seen in this hospital, in children for the most part under three years of age. Of this number 197 have been observed during the lumbar puncture period and are available for more careful analysis. Some valuable data obtained from the records of 103 earlier cases are introduced. In order to gain some idea of the relative frequency of the different forms of acute meningitis I have not included in the table cases seen before lumbar punctures were regularly made nor cases of cerebrospinal meningitis observed during the epidemic which ended in the spring of 1906, so that I think the figures which follow may be taken as fairly representing the usual conditions.

Etiologically, the 197 cases are divided as follows:

Tuberculous	138
Pneumococcus	22
Meningococcus (sporadic)	24
Staphylococcus or streptococcus	10
Bacillus influenzae	4
Colon bacillus	1
	199
Counted twice, mixed infections	2
	197

In other words, apart from epidemics of cerebrospinal meningitis, 70 per cent. of the cases of acute meningitis occurring in young children are tuberculous. The objection may perhaps be raised that hospital figures are not to be taken as representing conditions which obtain generally. The admissions to the Babies' Hospital are, however, from every class, and I think this criticism will not hold.

During the last five years lumbar puncture has been performed about one thousand times. After simple lumbar puncture no accidents have occurred; there have been no alarming symptoms, and no case of infection. However, in a single instance in which repeated injections were made in a case of cerebrospinal meningitis for the injection of Flexner's serum, secondary infection did occur, in spite of routine aseptic precautions. This is a warning which should be heeded. In another child suffering from cerebrospinal meningitis an alarming collapse followed the injection of 35 c.c. of serum. The fluid was warmed and the injection made in the usual manner, but the child came near dying and was rescued only after the most strenuous efforts. Aside from these two cases my experience has been without special incident. Too much, therefore, can hardly be said in favor of a systematic resort to lumbar puncture as a means of diagnosis in cases of meningitis; but it is a procedure requiring considerable skill and necessitating as strict asepsis as any surgical operation.

SIMPLE MENINGITIS

Before passing to a consideration of the different groups of cases which have been enumerated, I should like to say a word concerning "simple meningitis," a term formerly much used and one which still figures largely in vital statistics. In most such reports three forms of meningitis are given: tuberculous, cerebrospinal and simple. Some give only tuberculous as a separate class, combining cerebrospinal and simple. In the U. S. Census Report of the registration area for 1908 there are mentioned 71,229 deaths from meningitis in the five years 1904-1908; 25 per cent. of these are classed as cerebrospinal; 26 per cent. as tuberculous, and 49 per cent. as "simple or unqualified." In this same report, of 6,902 cases of meningitis occurring in the first three years of life in the year 1908, 32 per cent. are classed as tuberculous. In the New York City report for 1908 there are recorded in children during the first three years of life, 819 deaths from meningitis, divided as follows:

Tuberculous	448 or 55 per cent.
Cerebrospinal	188 or 23 per cent.
Simple	183 or 22 per cent.

Previous to the period here considered the diagnosis of "simple meningitis" appears in the hospital records in twenty-three cases. It was at that time our custom to contrast such cases with those which were tuberculous. At present the group "non-tuberculous" meningitis has been pretty well differentiated. The term "simple meningitis" has no longer any significance and should be dropped. There is not the slightest doubt that the largest proportion of cases so classified belong in the tuberculous group. From experience in the hospital, where careful differential diagnosis of the different forms of meningitis has been possible by lumbar

puncture, it is evident that tuberculous meningitis is very much more frequent than would appear from vital statistics of the country generally, or even those of New York City, and that a large number, probably the great majority of the cases put down as simple meningitis, and many of those recorded as cerebrospinal, are really tuberculous.

COLON MENINGITIS

Beginning with the smallest group I wish first to mention a case of meningitis due to a bacillus of the colon group which occurred in a baby only four weeks old. The child was admitted for an Erb's palsy and malnutrition. The usual symptoms of meningitis developed: temperature up to 103 F., leukocytosis of 13,000, general hyperesthesia and rigidity. A purulent fluid was drawn by lumbar puncture which showed a pure growth of a bacillus of the colon group. The illness lasted ten days. There were no symptoms pointing to visceral lesions elsewhere, but no autopsy could be obtained. In private practice I have seen one other case of meningitis in which the only growth from the cerebrospinal fluid was a bacillus of the colon group. This also occurred in an infant four weeks old, who had previously suffered, it was reported, from a urinary infection due to the colon bacillus. The child recovered from the acute symptoms, but developed a secondary hydrocephalus.

INFLUENZA MENINGITIS

Thus far four cases of meningitis due to the *Bacillus influenzae* have been observed; all of which have occurred during the last year. Clinically this form resembles the meningococcus cases and it is only by lumbar puncture that a differential diagnosis can be made. These cases are not common. I have seen but one other in private practice. Dr. Flexner tells me that he has had a considerable number of fluids sent to him with clinical diagnosis of cerebrospinal meningitis which contained only the influenza organism. All these ended fatally, as well as those which have been personally seen. It is my belief that this is the almost invariable termination. In three of the four cases that have come under my observation the *B. influenzae* was obtained by cultures from the bronchial secretion during life, and in two, in which examinations were made, it was also obtained by culture from the nasopharynx. This would suggest the nasal mucosa as the port of entry. In three cases examined the organism was found in the blood. One recent case had some features of unusual interest. An infant of eight months was admitted to the hospital with an acute abscess of the left elbow. Cultures from the pus on ordinary media gave no growth; however, on blood-agar a pure growth of the *B. influenzae* was obtained. The child shortly after developed acute men-

ingitis and died from the disease. The cerebrospinal fluid during life and the cultures from the meningeal exudate at autopsy showed a pure growth of the *B. influenza*.

MENINGITIS FROM PYOGENIC ORGANISMS

The common pyogenic organisms, streptococcus and staphylococcus, have been very infrequently found by me as the cause of meningitis. They were present in but ten cases. In one other a streptococcus infection complicated a tuberculous case. It is rather striking that six of the ten cases occurred in newly-born children, and that in five the meningitis was secondary to spina bifida. In one it followed an operation on a hydrocephalus, and in only two cases did it occur under conditions resembling a primary inflammation. In one case, in an infant three months old, the autopsy showed encephalitis as well, and the streptococcus was also found in the heart's blood and lungs.

Clinically this form of meningitis was characterized by severe general and local symptoms and a rather rapid development, with always an unfavorable termination. Since so much has been made in medical literature of the association of otitis media and mastoiditis with acute meningitis, my experience on this point may possess some interest. I saw meningitis develop but once after otitis or its complications. This patient was a baby fifteen months old who had had a double mastoid operation done in Europe. Dressings had not been changed from the time the child had sailed until she was admitted to the hospital, a period of nearly two weeks. At that time they were very foul and the wound in bad condition, and the child desperately ill. Symptoms of acute meningitis developed and the child died in the course of a few days. The autopsy, however, showed the meningitis to be a tuberculous one. A careful examination showed no connection whatever between the mastoid lesion and the one in the meninges. My experience leads me to question whether the dangers of meningitis from cases of otitis or mastoiditis are as great as they have been represented. I have always in the hospital wards many cases of acute otitis and a moderate number of these patients develop mastoid complications. However, on by no means all of them is the mastoid operation done. I am, therefore, led to the opinion that so far as patients of this age, chiefly under two years, are concerned, meningitis from a neglect to perform the mastoid operation is one of the rarest occurrences.

MENINGOCOCCUS MENINGITIS

It is not my purpose to enter minutely into a study of the twenty-four sporadic cases of cerebrospinal meningitis which have occurred since the great epidemic nearly five years ago. The number is too small to admit of any generalizations. Fourteen children received serum treatment, of

whom six recovered and eight died. The deaths included one chronic case in which the patient was injected in the third month when in a hopeless condition. Another was one of the first patients to be treated by the serum; in this case only a single small dose was administered. One child was improving but died from intercurrent measles. Two children, one an infant of five weeks and another of nine months, died of marasmus after all symptoms of acute meningitis had subsided. One child at first improved very much under the injection of the serum, and all the organisms disappeared from the fluid, but the child steadily lost ground and died, the autopsy showing an encapsulated meningeal abscess at the convexity, containing fully half an ounce of pus which, by culture, showed the meningococcus. One child died suddenly a week after all acute symptoms had passed. No autopsy could be obtained. Death in one instance was due to secondary infection with the staphylococcus.

In several of our cases which ended in recovery the nervous symptoms were slow in disappearing. Inability to support the head sometimes existed for two or three months, and in two cases evidence of a moderate intraventricular effusion persisted for several weeks, but finally disappeared. I have been struck with the irregularity exhibited by these cases in infants, by the slowness of recovery and by the large doses of the serum required in those who did get well.

Of ten patients who received no serum, three recovered and six died; one was discharged unimproved and doubtless died soon after.

PNEUMOCOCCUS MENINGITIS

Twenty-two cases of pneumococcus meningitis were observed, or about 11 per cent. of the entire number. Of these, thirteen patients had definite pneumonia with consolidation and four of these had also empyema. One patient had pulmonary tuberculosis. Of the eight remaining patients nearly all had some pulmonary signs and symptoms, evidences of bronchitis at least. The diagnosis was confirmed by autopsy in eleven of the twenty-two cases. In twenty the pneumococcus was found in the cerebrospinal fluid; one of the two remaining cases coming to autopsy.

The histories of the two patients in whom lumbar puncture gave negative results have already been published¹ but are sufficiently interesting to refer to again. While in only one of these was the diagnosis established by an autopsy, the symptoms in the second case were so similar that the diagnosis seems reasonably clear, though not positively proven.

The first was a child 20 months old whose attack came on with repeated convulsions, fever and a leukocytosis of 24,000. For one week the symptoms were those of a fairly typical acute cerebrospinal meningitis except for the absence of rigidity of the neck and extremities. Puncture made on the first day and repeated on the seventh day gave a perfectly

1. Arch. Pediat., March, 1908.

clear fluid. No organisms of any kind could be discovered in the smears or by culture. During the third week the patient developed pneumonia with consolidation; and the persistence of the nervous symptoms led to a third puncture which, like the other two, gave negative results although the amount of fluid removed was large—105 c.c. After six weeks all the acute symptoms subsided and the condition resembled one of a mentally defective child with slow wasting. Death occurred in the eleventh week from a second attack of pneumonia. The autopsy showed an old meningitis at the convexity; from this exudate a pure growth of the pneumococcus was obtained. The base of the brain was normal.

The second case occurring in a child 15 months old was almost the counterpart of this first one, but ended in partial recovery. Three punctures were made, in all of which the fluid was negative. Pneumonia developed in the fourth week but cleared up. Active nervous symptoms continued for four weeks, then gradually passed away. When discharged from the hospital the patient could not sit up nor support the head. Vision and hearing seemed absent. Six months later the patient was seen again. There had been considerable improvement, but the child clearly was mentally defective.

It seems evident that there was in both of these cases some involvement of the cortex in the inflammatory process; but no paralysis occurred in either case. Neither in its symptoms nor in its course did the disease suggest the cerebral form of poliomyelitis. We are accustomed to place so much reliance on lumbar puncture that the possibility of the existence of acute meningitis with a normal fluid is rather difficult to grasp.

Clinically, pneumococcus meningitis is shorter than any of the other forms, possibly excepting that due to influenza. In eight of the twenty-two cases it lasted three days or less; and in two-thirds of the entire number it was six days or less. It presents greater difficulties of diagnosis than any of the other forms; in the first place for anatomic reasons. The lesion is usually most marked at the convexity and may be limited to that part of the brain. The diagnosis of a convexity meningitis is proverbially difficult, for many of the most characteristic signs such as opisthotonos, irregularity of pulse and respiration, cranial-nerve involvement and distention of the fontanel, are usually wanting. Again, pneumococcus meningitis has been in my experience seen in younger patients than either cerebrospinal or the tuberculous form. Half of our cases occurred in infants under six months old, and two-thirds were under nine months. It has long been my belief that pneumococcus meningitis, like pneumococcus pericarditis and peritonitis, was the result of a generalized pneumococcus infection occurring much more frequently in very young patients than in those who were older. This has been confirmed by finding the pneumococcus in the heart's blood in every one of seven cases of pneumococcus meningitis in which cultures have been made.

TUBERCULOUS MENINGITIS

I have already said that 70 per cent. of my cases of acute meningitis, apart from the epidemic of cerebrospinal meningitis, were tuberculous. Its great frequency I am sure is not appreciated. During the past four years 8 per cent. of the deaths in the Babies' Hospital have been from this cause. I may have overlooked some cases but I think not many; for autopsies are obtained in this institution in nearly 50 per cent. of the fatal cases, which is a larger proportion than in any other hospital of the City so far as my knowledge goes. Besides, every suspected case receives lumbar puncture and the cerebrospinal fluid is examined both microscopically and by culture. We may safely say that none have been wrongly diagnosed, for in all but two cases bacilli have been found.

In general practice tuberculous meningitis is certainly very often overlooked or a mistaken diagnosis made. Of thirty successive cases admitted to the hospital, in only three was the diagnosis of tuberculous meningitis previously made and in only three others was it suspected. The most common diagnosis with which the child was admitted was either some gastric disorder or cerebrospinal meningitis.

There are two common misconceptions regarding tuberculous meningitis: the first is that it is a disease of long duration, often lasting two or three months or even longer. I have never seen tuberculous meningitis last over five weeks, and only once have I seen it last five weeks, this in a child of nine years. Of the cases reported in this paper, in infants chiefly, the average duration has been about two and a half weeks after the first definite symptoms of illness appeared. A second error is that tuberculous meningitis usually affects delicate infants, those suffering from malnutrition, often of the marasmus type. The inference is drawn that because a child with symptoms pointing to meningitis was previously in good health, the process could not be tuberculous. It is my experience both in hospital and private practice that the vast majority of these patients have been, previous to their attack, apparently in as good health as any children whom I see. Not that very healthy infants are more prone to tuberculous meningitis than others, but that a tuberculous infection of a young child is very apt to involve the brain early, before there is time for the symptoms which result from a general tuberculosis to be manifest. Some reasons for this will appear later.

Seasonal Prevalence.—That tuberculous meningitis occurs more at one season of the year than at another has not, so far as I am aware, hitherto been noted. For the last two or three years I have been struck with the fact that more patients were admitted during the spring months than at other times and I have had the earlier records of the hospital searched to ascertain the month when patients were admitted.

Chart 1 shows by months the time of admission of 218 patients in the Babies' Hospital service. It will be noted that the curve is at its lowest during the summer and early fall; that there is a slight rise in December and January, but a very sharp rise in the spring months, the highest point being touched in the month of April; the number of cases in the spring months of March, April and May being about twice as great as were seen at any other similar period during the year. A steady fall is noted during the summer until October is reached.

The explanation for this variation is not altogether clear. The most plausible one seems to be that these infants have been infected some time previously and are carrying a latent focus somewhere in the respiratory tract, usually the bronchial glands. Under the influence of acute respira-

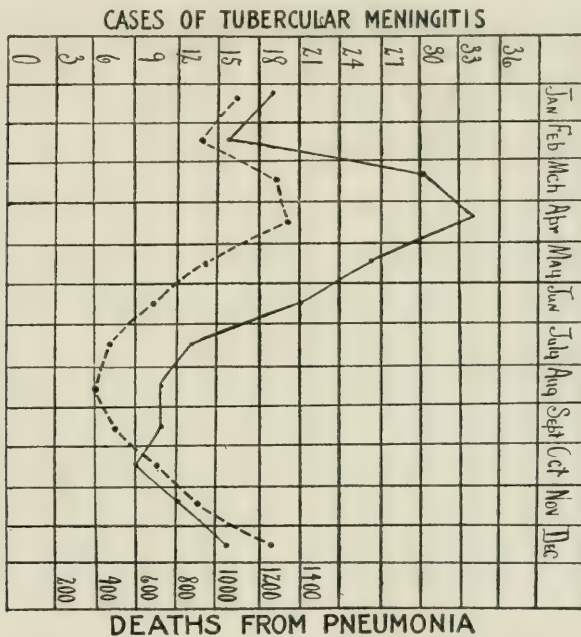


Chart 1. The upper curve represents the seasonal occurrence of 218 cases of tuberculous meningitis; the lower curve represents the deaths from pneumonia in New York City for one year.

tory infections occurring during the winter and spring months, the latent tuberculous disease becomes an active process and a rapidly spreading infection occurs; for in none of these infants is the brain lesion the only one. At autopsy pulmonary lesions are almost invariably found; and miliary tubercles are usually present in many other organs. This indicates that the meningitis in infants is a part of a generalized infection and causes death before the other evidences of the disease are usually manifest. Some of these children showed a few scattered râles in the chest:

and, still more infrequently, evidences of more serious pulmonary disease were present; but the great majority of them showed no pulmonary signs of disease whatever.

An attempt has been made to see in how many cases of tuberculous meningitis bacilli could be found in the sputum. In many it has been difficult to secure any proper sputum for examination. Yet in 116 patients in whom the effort was made, bacilli were found in forty-nine. These cases were taken routine, not selected because of the presence of pulmonary signs or symptoms. It is true that the number of bacilli is seldom large and unless careful and sometimes repeated examinations are made, they are likely to be missed. Yet when present they were found

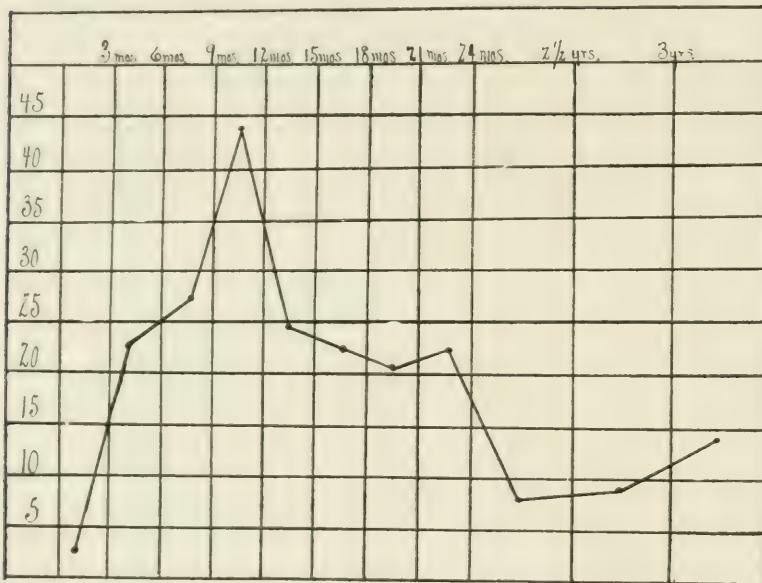


Chart 2. The age incidence in 218 cases of tuberculous meningitis.

at the first examination in three-fourths of the cases, although in one case, not until the sixth examination.

The close association of tuberculous meningitis with inflammations of the respiratory tract is also suggested in the accompanying chart. The lower curve in Chart 1 shows the deaths from pneumonia in New York City for 1909. The similarity of these two curves is certainly striking. I do not think that the tuberculous meningitis in older children would show so close an association with pulmonary disease as is true in infancy.

Age Incidence.—Chart 2 shows the age incidence. Inasmuch as the Babies' Hospital admits children up to three years of age the curve I think may be taken to represent pretty accurately the occurrence of the disease in patients below that age. Only three patients under three

months of age were seen; the greatest number of patients were seen between the ages of nine and twelve months, a rapid decline in the curve being noted after the first year. This is a striking fact, but the reason for it is not very clear. The greater frequency of tuberculous meningitis in children from nine to twelve months of age may be due to the closer exposure of young infants to infected adults than occurs with children who are somewhat older. It is possible also that a closer exposure occurs in winter than in summer and that this may have some bearing on the greater frequency of the disease in the spring months. The incubation period is at present unknown. It seems probable that in most cases it is several weeks at least.

Source and Type of Infection.—It is my experience that nearly all the cases of tuberculous meningitis, the source of whose infection we have been able to trace, have their origin in exposure to adults with pulmonary tuberculosis. A striking confirmation of this is shown in the results of the observations made by Dr. W. H. Park in the Research Laboratory of the Health Department on thirty-two cases in my series in which the type of bacillus was worked out. In thirty it was of the human type; in one it was of the bovine type; in one case both types were present.

The von Pirquet Reaction.—The statement frequently has been made in medical literature that comparatively few infants with tuberculous meningitis respond positively to the von Pirquet test. Systematic observations on this point have been made during the past two years. Of sixty-five cases a positive reaction was obtained in fifty-one; a negative in eleven, and doubtful in three. Of the fourteen cases that were negative or classed as doubtful, four patients were moribund and seven extremely prostrated and with feeble circulation. In the remaining three there was no apparent reason why a reaction should not have been obtained. I regard the skin test, therefore, as of very great diagnostic value, and a negative result, except in the conditions just mentioned, of much diagnostic importance.

I have attached so much importance in recent times to the von Pirquet test and the findings of the examination of the cerebrospinal fluid, that negative results in either of these I have come to regard as very significant. A baby seven months old was admitted with a fairly typical history of tuberculous meningitis: onset with vomiting, slight fever, convulsions developing in three or four days; drowsiness merging into stupor; marked constipation. The prominence of the fontanel was so great that the mother herself had noticed it and, in fact, the "lump on the head" was one of the reasons why the child was brought to the hospital. Lumbar puncture was made and 120 c.c. of perfectly clear fluid removed. It was under very high tension. So confident was I that this was a case of tuberculous meningitis that the search for the bacilli in the cerebrospinal

fluid was continued for several hours, but with negative results. Greatly to my surprise the child did not respond to the von Pirquet test, but what was still more unusual, the child promptly recovered and at the end of a week was discharged to all appearance quite well. It died about one month afterward rather unexpectedly, but without cerebral symptoms, so the visiting nurse learned. I have seen an almost identical picture in another child, in whom recovery was complete and permanent. The explanation of these is rather difficult without assuming the existence of a primary acute serous meningitis, regarding which I have always been rather skeptical.

CONCLUSIONS

Lumbar puncture has placed the diagnosis of meningitis on a new basis. It should be employed in every suspected case. It is only with very rare exceptions that to a skilled observer it gives uncertain results.

Nearly three-fourths of the cases of acute meningitis in young children are tuberculous, except when cerebrospinal meningitis is epidemic.

In tuberculous meningitis bacilli are always present in the cerebrospinal fluid; although difficult to find in the early stages, in the later stages a careful examination should discover them. The von Pirquet test in most cases gives positive results.

In infants and very young children tuberculous meningitis occurs usually as an early manifestation of a general tuberculosis, and generally causes death before the lesions elsewhere are far enough advanced to give definite signs or symptoms. Pulmonary lesions are present in nearly all cases.

Tuberculous meningitis is of human origin. Altogether the most frequent cause is exposure to adults with pulmonary tuberculosis.

The age incidence and the seasonal occurrence are points which are not yet fully explained.

Pneumococcus meningitis usually occurs in younger patients and is associated with pneumonia. Clinically it resembles meningococcus meningitis but usually the course is shorter. It is almost invariably fatal.

Influenza meningitis is infrequent and also resembles the cerebrospinal form. It is almost invariably fatal.

Streptococcus and staphylococcus meningitis are very rare forms in infancy, usually occur in the new-born and are often associated with spina bifida. Under such circumstances they are always fatal. From mastoid disease this form is seldom seen in young children.

Meningococcus meningitis is really the only variety in which at present there may be said to be any hope of recovery. The results in this variety of meningitis have been very greatly improved by the serum treatment.

THE CONSTANT PRESENCE OF TUBERCLE BACILLI IN THE CEREBROSPINAL FLUID OF TUBERCU- LOUS MENINGITIS

WITH OBSERVATIONS ON THE CEREBROSPINAL FLUID IN OTHER FORMS OF
ACUTE MENINGITIS *

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A systematic effort has been made since March, 1906, in the laboratory of the Babies' Hospital, to determine the presence of tubercle bacilli in the cerebrospinal fluid in cases of tuberculous meningitis. One hundred and thirty-eight patients have been admitted to the wards of the hospital since that time, but fluids for examination were obtained from 137 only. In all but two, tubercle bacilli were demonstrated in the cerebrospinal fluid. The technic which was followed in demonstrating the bacilli has given such satisfactory results that it is herewith given in detail.

TECHNIC

The cerebrospinal fluid is collected in several test tubes, allowing about 20 c.c. to a tube. The last fluid withdrawn after the child has been raised to the sitting posture is considered the most important, as the bacilli are usually found more readily in this. Care must be taken not to shake the tubes. It has been found that a fibrin coagulum, the so-called "film," forms more often in tubes which have not been agitated. The fibrin coagulum is at first very delicate and friable. It forms with greater regularity and becomes firmer in fluids which have been placed in the incubator over night. After ten hours it is usually so firm that the entire film can be removed with a platinum loop. It is then carefully spread with fine needles on a glass slide. This is stained by the carbol-fuchsin Gabbett method. Bacilli were found with comparative ease in every case in which the film formed. In several cases in which the question of immediate diagnosis was extremely important, there was a sufficient coagulum after the fluid had stood three hours to enable one to find the bacilli.

In about 4 per cent. of the fluids examined this coagulum did not form at all. One of the following devices was then used: The sides of the test tubes were scraped with a platinum loop and any material

*From the Laboratory of The Babies' Hospital, New York.

removed, superimposed, drop by drop, over a small area on a glass slide, each drop dried in the air and fixed in the flame before another was added. Or with a fine capillary tube, the sediment from the test tube was superimposed in the same manner. In a few cases the sediment from centrifuged fluid was used. If the fluid drawn early in the disease showed no coagulum and if no bacilli were found, then at the second puncture, before the needle was withdrawn, it was pushed slightly forward so as to touch the anterior surface of the spinal canal, and one or two drops of blood allowed to flow into the last fluid withdrawn. With the addition of the blood a coagulum would often form, when the other tubes of fluid, drawn at the same time, remained clear.

The length of time required to find the tubercle bacilli varied greatly in different cases. Often they were found in a few minutes. If not readily discovered, careful search through the entire film was made. When a moderate number of bacilli were present, a thirty to forty minute search was usually rewarded by the finding of isolated organisms or several in clumps. In no case was a single bacillus considered conclusive. The films from all the tubes sometimes had to be used, and the bacilli were then found after a two- or three-hour search. The average time consumed was about an hour. The amount of fluid removed has averaged 60 c.c. although frequently twice as much has been obtained.

FINDINGS

The cerebrospinal fluid in tuberculous meningitis is usually as clear as distilled water, and often, although not invariably, there are seen floating in it, very small white flecks. In only one case was there a distinct cloudiness. In this the film showed far more polymorphonuclear cells than usual, and also a very large number of tubercle bacilli in each field. Repeated cultures and examinations made in this case, however, revealed the presence of no other organism. In all the other cases the predominating type of cell was the mononuclear, with very few scattered polymorphonuclear cells.

Of the 138 cases of tuberculous meningitis, tubercle bacilli were found in the fluids of 135. Of the remaining three, in one only was an early puncture possible, because the child was removed from the hospital during the first week of illness. No bacilli were found in this fluid, but a guinea-pig was inoculated and eight weeks later showed characteristic lesions of tuberculosis. Another child was brought to the hospital moribund. The diagnosis of tuberculous meningitis was evident from the history obtained from the physician. Only 2 c.c. of clear fluid could be obtained by lumbar puncture, not enough for a satisfactory examination. In the third case no puncture was made, as the child died a few minutes after admission. The diagnosis rested on the clinical symptoms.

Bacilli were therefore missed but once when a satisfactory amount of fluid could be obtained for examination, and that was from a puncture made very early in the disease.

There is little doubt that the bacilli are more numerous late in the disease, yet they were found in the first puncture in 117 cases; in the second in thirteen; and in the third puncture in four cases. Most hospital patients are not admitted until symptoms are tolerably well marked. It is therefore somewhat difficult to say how early in the disease bacilli may regularly be found. On the average, the first puncture was made about ten days before death. The larger amount of fibrin found in the fluid late in the disease, as evidenced by the constant formation of a film, renders the discovery of the bacilli easier at that time. The four cases in which a third puncture was necessary were admitted with symptoms suggesting meningitis. The early puncture showed only an excess of clear fluid, under slightly increased tension, and a few mononuclear cells.

FINDINGS IN OTHER FORMS OF MENINGITIS

Examination of the cerebrospinal fluid was made in twenty-two cases of pneumococcus meningitis. The fluid in twenty of the cases could not have been distinguished macroscopically from turbid fluids in other forms of meningitis. It varied from a slight cloudiness to such a turbidity as to cause a thick deposit of pus in each tube. The cells were chiefly polymorphonuclear; the organisms were plentiful in the smears, and grew readily in cultures.

In contrast to these typical cases, it may be of interest to mention the findings in some other cases, which were quite exceptional. A child with lobar pneumonia showed definite meningeal symptoms. An excess of clear fluid under increased tension was obtained twice by lumbar puncture, and from both fluids the pneumococcus was grown in pure culture. The disease terminated by crisis, the nervous symptoms disappearing with the fall in temperature, the child making a prompt recovery. The case was certainly not one of meningitis.

In twelve other cases of pneumonia with very pronounced nervous symptoms, punctures were made, but in none was the pneumococcus found. In cases of pneumonia with a high temperature, if a puncture was made, the cerebrospinal fluid was usually found to be under increased tension and in excess of the usual amount. This has later been observed to be true in many other diseases in which lumbar puncture has been done on children with nervous symptoms suggesting meningitis, the true diagnosis being made later. In one case, which was proved by autopsy to be one of pneumococcus meningitis, three punctures showed normal fluid in the acute stage. This finding, which was a very remarkable one, sug-

gests that one cannot draw the conclusion that because the cerebrospinal fluid is negative, there is no meningitis present.

The cerebrospinal fluid in the four cases of influenza meningitis all showed great turbidity, the cells were practically all of the polymorphonuclear variety, and the influenza organism was readily cultivated. An examination of a smear from the fresh fluid shows at once that the organism is not the meningococcus, and a culture on blood agar should therefore immediately be made. Cultures on ordinary media would show no growth and one would easily be misled if one relied on them. The organisms are not numerous in the smears, in marked contrast to the great numbers of organisms in cases of pneumococcus meningitis.

In a series of twenty-four meningococcus cases, the fluid from twenty-two showed the usual turbidity, great numbers of polymorphonuclear cells and the presence of the meningococcus in the smears and by culture. In two cases the findings were unusual. One was that of a six months old child admitted in the second week of illness with a history strongly suggesting meningitis. By lumbar puncture 15 c.c. of clear fluid was obtained, which was negative by smear and culture. A very few polymorphonuclear cells were found. The fever and nervous symptoms increased with such severity that a second puncture was made seven days later, and 20 c.c. of slightly turbid fluid obtained, in which the meningococcus was easily demonstrated. From this time the course of the disease was that of a rather mild cerebrospinal meningitis.

An almost identical history was that of a nine months old child, admitted after an illness of four weeks. The symptoms were rather indefinite. The first puncture in this case also showed clear fluid and no organisms of any kind could be found. Two weeks later the fluid was that of a typical cerebrospinal meningitis and the meningococcus was grown from fluids obtained at four subsequent punctures. From a study of these histories the question arises whether there may not be a definite meningeal inflammatory lesion present with, at the same time, a clear cerebrospinal fluid from which no organisms can be cultivated.

In the ten cases of streptococcus meningitis the fluid from each showed great turbidity. There were many polymorphonuclear cells present. The streptococci were present in large numbers and grew readily on ordinary media.

There were three cases in which more than one type of organism was found. In one case tuberculous meningitis occurred six weeks after recovery from a meningococcus meningitis. In another, tubercle bacilli and streptococci were both present during the acute stage. In the third, pneumococci and meningococci were both isolated from the thick, purulent fluid.

OTHER TESTS OF CEREBROSPINAL FLUID

Tests with Fehling's solution were made on 111 fluids to determine the diagnostic value of the presence of a reducing substance. The results were so inconstant that no reliance could be placed on this test in differentiating between tuberculous and other forms of acute meningitis. The results are embodied in the following table:

Form of meningitis	No		Total
	Reduction	Reduction	
Tuberculous	24	26	50
Meningococcus	3	29	32
Pneumococcus	2	2	4
Streptococcus	.	1	1
Normal fluids	23	1	24

These findings suggest that a reduction in normal fluids is the rule, and yet there is reduction in so many cases of tuberculous meningitis that the test is of no value in diagnosis.

The globulin test of Noguchi has been used only recently. It consists of a precipitation of an excess of globulin by means of a solution of butyric acid in normal salt solution, and the addition of a sodium hydrate solution. Seventeen cases of meningitis—eight tuberculous, five meningococcus and four influenza—all gave typical positive reactions. Of twenty-two normal fluids tested, all but two gave a negative reaction. Of the two apparently normal fluids giving a positive test, one was from an acute case of enterocolitis with toxemia and a temperature of 107 F. The cerebrospinal fluid, which was clear, was injected into a guinea-pig and ten weeks later no evidence of tuberculosis or other disease could be found. The other fluid was also from a case of colitis, the autopsy in which showed no meningeal lesion. This test appears to be of great value in differentiating normal from abnormal fluid.

INFLUENZAL MENINGITIS AND ITS EXPERIMENTAL PRODUCTION *

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The extension of the practice of employing lumbar puncture as an aid to the diagnosis of meningitis has had, as one effect, the establishment of the important fact that the influenza bacillus is a not infrequent cause of sero-purulent meningitis. That the influenza bacillus may act as a cause of acute inflammation of the meninges has been known since the publication of Pfuhl's¹ illustrative cases in 1892, but that it acts as a not infrequent cause of that condition we are just beginning to learn. Influenzal meningitis appears to be a very severe and highly fatal form of meningitis and to be exceeded in respect to its fatality only by the pneumococcus and tuberculous forms. It remains, however, for the present, an undecided question whether influenza bacilli may not occur in the cerebrospinal fluid without setting up inflammation, just as pneumococci and some other organisms have been known to do. The frequency with which influenza bacilli occur in the cerebrospinal fluid in all conditions has not yet been determined.

There have come under my observation within the past year eight cases of influenzal meningitis, from which the influenza bacillus was isolated in every case from the fluid removed by lumbar puncture, and the cultures studied in respect to their biologic reactions. All the cases terminated fatally.

TECHNICAL METHODS

The influenza bacillus is a slender rod, somewhat varying in size, staining deeply at the poles, and being Gram-negative. Its invariable and most prominent characteristic is its hemophilic property, next to which pleomorphism is its most striking attribute. It may be considered as conclusively established that a pseudo-influenza bacillus, as distinct from the true influenza bacillus, producing pathologic conditions in human beings, does not exist.

The cultivation of the influenza bacilli dealt with in this paper was made exclusively on agar mixed with rabbits' blood. Petri plates and slanted tubes of the medium are readily prepared by adding a few drops

* From the laboratories of the Babies' Hospital and of the Rockefeller Institute.

* Read before the joint meeting of the Section on Pediatrics of the New York Academy of Medicine and the Philadelphia Pediatric Society, Dec. 8, 1910.

1. Pfuhl: Berl. klin. Wchnschr., 1892, xxix, 979 and 1009.

of the rabbit's blood to the melted agar, previously cooled to 45 C. I to use rabbits instead of pigeons for securing the blood, because of the greater ease with which considerable quantities of blood can be obtained from the rabbit. It was found that when the blood was mixed with the agar, a better growth of colonies could be secured, and they could be studied more readily. It was preferred to counterstain the Gram preparations of the bacilli with 10 per cent. aqueous safranin, since that stain brought out plainly the poled extremities.

It has been the custom at the Babies' Hospital for the past two winters to take cultures on blood-agar plates from the pharyngeal and bronchial secretions of almost every child admitted during some period of its stay in the hospital. When patients came to autopsy routine cultures on blood-agar were prepared from both lungs and the blood of the heart. In this way we have collected a considerable number of different cultures and strains of the influenza bacillus and numerous data on its occurrence in the body of children during life and after death.

CLINICAL CASES OF INFLUENZAL MENINGITIS

Within a little more than a year, specimens of cerebrospinal fluid from eight cases of influenzal meningitis have come into my hands for study. In some instances, the fluid was sent to the Rockefeller Institute to be examined for *Diplococcus intracellularis* and the influenza bacillus was discovered accidentally. In other cases, the patients were admitted to the Babies' Hospital, where the fluids were examined and in one case an autopsy was performed.

CASE 1.—The turbid fluid obtained by lumbar puncture from this case was sent to the Rockefeller Institute by Dr. Agar who, in association with Dr. Avery, has already published an account of it.² Film preparations prepared from the fluid showed a large number of Gram-negative bacilli, some of which were very small, some quite plump and larger. Cocci were absent. Polymorphonuclear leukocytes were present in numbers, a few of which had taken up the bacilli. No growth of the organisms was obtained on plain or serum-agar, but cultivation was successful on blood-agar, on which small, moist translucent colonies developed. These were composed of minute, slim bacilli. There was entire absence of the larger plump forms but the latter, together with some longer, curved bacilli, appeared in the cultures forty-eight to seventy-two hours old. They represented involution forms, since the plates showed the growth to be pure.

CASE 2.—About 3 c.c. of turbid fluid obtained from a child 3 years old was sent to the Rockefeller Institute for examination from the Lebanon Hospital. Flakes of thick pus occurred in the fluid and adhered to the sides of the test tube. Cover-slips showed many polymorphonuclear leukocytes, some of which contained small Gram-negative bacilli. Outside the leukocytes, smaller bacilli were numerous. The bacilli were, for the most part, short, but some moderately long threads occurred. No growth took place on plain or serum-agar, but a characteristic growth was obtained on the blood-agar.

CASE 3.—About 6 c.c. of very turbid cerebrospinal fluid obtained from a child 2 years old was sent to the Rockefeller Institute for examination. Film preparations showed many polymorphonuclear leukocytes and numerous short Gram-

2. Arch. Pediat., 1910, xxvii, 284.

negative, poled, regular bacilli. Rarely were the bacilli found within the leukocytes. The organisms did not grow on plain or serum-agar, but did grow on blood-agar.

CASE 4.—About 50 c.c. of very turbid fluid was obtained from a child about 4 years of age which, on standing, deposited a thick layer of pus. The film preparations showed numerous polymorphonuclear leukocytes and very large numbers of Gram-negative minute, regular, poled bacilli. A very few thread forms occurred. Blood-agar cultures gave a pure growth. A second specimen of the cerebrospinal fluid, more purulent than the first, gave a similar culture in result. The cultures of the influenza bacilli were obtained also from the nasopharynx.

CASE 5.—A child, 6 months old, admitted to the Babies' Hospital. There was a history of convulsions and rigidity for two days, following a period of two weeks of fever and cough. Fifteen c.c. of blood-stained cerebrospinal fluid were withdrawn and the influenza bacillus grown in pure culture. A second lumbar puncture yielded 10 c.c. of a more turbid fluid, from which pus was deposited. The film preparations showed many bacilli, consisting of long and curved, as well as short rods. Cultures on blood-agar were deposited from the second puncture fluid, as well as from the nasopharyngeal and bronchial mucus. No autopsy was permitted, but from the blood withdrawn from the heart one and a half hours after death, a similar bacillus was cultivated.

CASE 6.—A child, 2 years and 10 months of age, admitted to the Babies' Hospital four days after the onset of symptoms of meningitis. Several lumbar punctures were performed during the nine days the child lived, and from 15 to 75 c.c. were withdrawn at each puncture. The fluid originally was turbid, gradually became more so, and finally consisted of thick pus. The influenza bacillus was grown on blood-agar from each specimen of fluid. Death occurred on the thirteenth day of the disease. No autopsy was permitted, but blood obtained from the heart one hour after death yielded growth of the influenza bacillus. The mucus from the nasopharynx and from the bronchi also yielded growths of the bacillus.

CASE 7.—A child of 8 months, admitted to the Babies' Hospital after three weeks of illness. At the time there was swelling of the left elbow joint. Two days after admission symptoms of meningitis appeared. Lumbar puncture yielded 35 c.c. of turbid fluid, from which the influenza bacillus was cultivated. Pus aspirated from the elbow yielded a similar growth. Death occurred three days after the appearance of the meningeal symptoms and the autopsy showed extensive purulent leptomeningitis. The exudate was abundant along the superior longitudinal sinus, over the frontal lobes, the cerebellum, pons and medulla, and in the interpeduncular space. The exudate consisted of thick pus. The lateral ventricles were distended with turbid fluid, and pus covered the choroid plexus. The spinal cord was much less involved apparently, but it could not be examined throughout its length. The suppuration about the left elbow extended to the denuded surface of the humerus, the lower epiphysis of which had separated. The lungs showed the lesions of bronchopneumonia and congestion and a moderate amount of bronchitis and tracheitis. Pure cultures of the influenza bacillus were obtained at autopsy from the pus at the elbow and in the meninges, as well as from the heart's blood. The lungs yielded a growth of influenza bacilli and streptococci.

CASE 8.—A boy of 5 months admitted to the Babies' Hospital in a moribund condition. Lumbar puncture yielded 20 c.c. of very turbid fluid, forming an abundant purulent deposit. Film preparations showed polymorphonuclear leukocytes together with many minute, short and regular bacilli, some of which were in pairs. Very few had been taken up by leukocytes. These bacilli proved to be the bacilli of influenza. Blood removed from the heart by means of a syringe half an hour after death yielded a pure growth of *B. influenzae*. Mucus secured from the pharynx by means of a swab after death did not show this micro-organism.

PROPERTIES OF THE CEREBROSPINAL FLUID

The cerebrospinal fluid in the eight cases was, without exception, cloudy and deposited, on standing, a whitish or yellowish sediment, the supernatant liquid remaining somewhat turbid. In the cases in which the progress of the disease could be followed, it was noted that the fluid became successively more purulent and the sediment of pus heavier. Case 7 yielded, on the last day of life, thick pus.

As was to be expected with fluids of the characters described, they all showed, under the microscope, the presence of polymorphonuclear leukocytes in abundance. The number of influenza bacilli present was usually very large. The bacilli occurred free in the cerebrospinal fluid, as a rule, and there was very slight phagocytosis. The morphology of the bacilli varied greatly. In Case 1 the bacilli were long, curved, and the ends often clubbed, corresponding to the involution forms met with in old cultures. The fluid from this case showed but few of the characteristic small forms. In the fluid from Case 2, the bacilli formed long threads but, nevertheless, typical small forms predominated. The bacilli in the fluid from Case 4 were small and regular and agreed with the typical bacilli as seen in recent cultures. However, not only did small numbers of curved forms also occur, but some long threads as well. We observed no examples corresponding with the very long filaments described by Ritchie.³

It is of interest to compare the results described for the eight cases, which have come under my observation, with the statement made by Cohoe⁴ that the spinal fluid obtained by lumbar puncture from patients with influenzal meningitis may be quite normal in appearance and that influenza bacilli may be contained in these fluids and be overlooked in film preparations, unless carefully searched for. This statement would seem to stand alone, since all the other statements made in the literature of the subject are to the effect that the fluid obtained by lumbar puncture, once inflammation has been set up by the influenza bacillus, is cloudy. Haedke,⁵ indeed, reports a case of an adult, in which the fluid withdrawn one day was clear, and the next day, cloudy. Death occurred twenty-four hours after the second puncture, and the autopsy disclosed an epidural abscess and an early localized leptomeningitis. In this case, we must conclude that the clear fluid was withdrawn before the localized meningitis had developed and that the fluid became turbid as soon as inflammation of the meninges appeared. In another case, reported by Traileseu,⁶ the fluid obtained by lumbar puncture is described as transparent, but

3. Ritchie: *Jour. Path. and Bacteriol.*, 1910, xiv, 615.

4. Cohoe: *Am. Jour. Med. Sc.*, 1909, cxxxvii, 74.

5. Haedke: *München. med. Wehnschr.*, 1897, xlv, 806.

6. Traileseu: *Ref. in München. med. Wehnschr.*, 1902, xlix, 118.

the microscopic examination is stated to have shown a large number of polynuclear leukocytes together with small bacilli, some of which were within cells, others without cells. It is evident that this fluid could not have been strictly normal in appearance or that the bacilli were difficult to find. The case described by Cohoe⁷ was that of an adult who recovered and the fluid was stated to have been slightly turbid. It is, of course, possible that the influenza bacilli may be present in the cerebrospinal fluid without setting up a meningitis, in which case the fluid would be clear, provided the number of bacilli was not great. Future determinations will have to prove whether, in such a case, the protein content of the fluid is not increased, for which determination the use of Noguchi's butyric acid test, or some other test for protein, will have to be employed.

CULTIVATION AND MORPHOLOGY

An effort was made in connection with each of the fluids to cultivate the bacilli present in them on plain-agar, sheep-serum-agar and blood-agar. No growth was ever obtained on the first two media, but a growth was always obtained on the last one. At later intervals, attempts were made to cultivate the different strains on agar free from hemoglobin, but without success, even after eight months of cultivation on the blood-agar. The pleomorphism of the bacilli is brought out clearly by observing cultures from day to day. After growing for fifteen to twenty-four hours, all the strains showed the usual minute, regular bacilli, among which threads were sometimes present in small numbers. On the second day, the curved forms and longer threads had increased in number and the bacilli in thickness while, after seventy-two hours of growth, the usual bizarre forms were present. The degree, as well as the rapidity, with which pleomorphism occurred was increased by cultivating the bacilli on Bordet's⁷ potato-blood-agar. After twenty-four hours on this medium, the cultures showed large, curved, irregularly stained elements. It should be noted that the cultures from Cases 4 and 7, which proved to possess the greatest degree of virulence for rabbits and for monkeys, were made up of bacilli regular in outline and short in form. It was shown that the bacilli from Case 7 were equally virulent, whether obtained from the pus from the elbow joint, the cerebrospinal fluid, or the heart's blood.

ANIMAL EXPERIMENTS

The bacilli were inoculated into mice, guinea-pigs, rabbits and monkeys. Mice proved highly susceptible to small injections into the intraperitoneal cavity, whether of the cerebrospinal fluid or the pure cultures of the bacilli. It was not found possible to increase the virulence appre-

7. Bordet: *Ann. de l'Inst. Pasteur*, 1906, xx, 731.

ciably by passing the organisms through series of mice, although the average dose was found to be reduced in the ninth passage to about one-half the original fatal dose. The peritoneal cavity of these animals contained little exudate, the spleen was always swollen, and the lungs and kidneys congested. The bacilli could always be recovered in pure culture from the heart's blood, peritoneum, and other organs.

Guinea-pigs, weighing about 200 gm. each, succumbed in twelve to twenty-six hours from injections of from one-half to one culture. The peritoneal fluid of these animals was increased, as much sometimes as 8 c.c. could be withdrawn, and it was always turbid. Polymorphonuclear leukocytes and bacilli were numerous but phagocytosis rarely occurred. The spleen was increased to two to three times its normal size; the kidneys were congested and the lungs showed scattered areas of congestion and inflammation. The bacilli could be obtained in pure culture from the heart's blood and viscera, and from the surface of the pia of the brain and spinal cord. Guinea-pigs sometimes survived three or four days, at which time all the fluid had escaped from the peritoneal cavity and a thick fibrino-purulent exudate covered the liver, spleen, etc.

Rabbits of about 1,200 grams inoculated by injection of one culture, twenty-four hours old, into the ear-vein, succumbed in from fifteen to thirty-six hours. Small hemorrhages existed in the parietal peritoneum and within the serous coat of the intestines and beneath the capsule of the liver, pleura and other organs. The spleen was swollen and soft, the kidneys much congested, while the lungs always showed areas of hemorrhage and of inflammation (pneumonia). The membranes of the brain and cord were normal in appearance. Cultures of the bacilli could be obtained from the heart's blood, viscera, urine, and from the surface of the brain and cord. The bacilli were always present in the lungs, but mingled with other bacteria. The mucous membrane of the upper nasal cavities showed, as a rule, deep congestion, and from its surface large numbers of influenza bacilli were cultivated. Cultures from the nasal secretions were always made before the inoculation of the bacilli and influenza-like organisms were not found in them. This precaution was taken also to exclude the possibility of the presence of the "snuffles" bacillus described by Beck.⁸

The most important of this series of animal experiments are those which were conducted with monkeys. Indeed, we succeeded in producing in two species, namely, *Cercopithecus callitrichus* and *Macacus rhesus*, infection of the meninges, by injecting suspensions of influenza bacilli into the subdural space by means of lumbar puncture. Monkeys do not develop symptoms or the lesions of acute meningitis in all instances after the injection of the cultures. The result depends, chiefly,

8. Beck: Ztschr. f. Hyg., 1893, xv, 363.

on the virulence of the culture employed. When one or two cultures on blood-agar suspended in salt solution are injected in the spinal canal, there is no immediate effect, but the first symptoms appear in from six to twelve hours afterward. From the appearance of the first symptoms, the severity rapidly increases and death occurs in from thirty-six to forty-eight hours or somewhat later.

Lumbar puncture made at different periods showed, first, a turbid fluid containing many polymorphonuclear leukocytes and, later, a more opaque or purulent exudate. Within the fluid were many of the bacilli, usually free, but, in a few instances, within phagocytes. Cultures on blood-agar always yielded a pure growth. The autopsy showed purulent exudate along the superior longitudinal sinus and spreading laterally, a turbid exudate over the cord and base of the brain, and a marked exudate in the region of the cord about the site of inoculation. The smears prepared from various parts of the pia-arachnoid of the brain and cord showed varying numbers of bacilli. Cultures were also positive, including the upper nasal mucosa.

Sections showed a purulent leptomeningitis, both on the surface of the brain and within the sulci, as well as over the spinal cord. The exudate was massed chiefly about the blood-vessels. Innumerable bacilli occurred among the pus-cells, many of which were in a state of fragmentation.

Especial reference should be made to a *rhesus* monkey, although it belongs to a series of experiments on which I expect to report later. This animal survived the subdural inoculation of one culture of the influenza bacillus for twenty-seven days. It had entirely recovered from the meningitis which had been set up, the cerebrospinal fluid had become clear, and the bacilli had disappeared. The autopsy showed an empyema at the base of both lungs, the pus of which contained the influenza bacillus in pure culture. The bacilli were not isolated from the heart's blood, brain or spinal cord.

The results of the inoculation of monkeys into the subdural space of the spinal cord with virulent cultures of the influenza bacillus indicate that an experimental form of influenzal meningitis can be produced, which tends to run a rapidly fatal course, in this respect resembling the clinical disease occurring spontaneously in human beings. There is a further resemblance in the changes which occur in the cerebrospinal fluid and through which it first becomes turbid, and then purulent, and, further, in the relation of the bacilli present in the fluid to the cells. Neither in human beings nor in monkeys has phagocytosis occurred to any great extent. The two reports in the literature which bear especially on our experiments are those of Cantani⁹ and Ritchie.³ Cantani injected

9. Cantani: *Ztschr. f. Hyg.*, 1896, xxiii, 265.

influenza bacilli into the brain in rabbits. He observed that non-lethal doses set up a chronic meningitis and sometimes led to the appearance of pus in the ventricles. The bacilli were present and demonstrable by culture and by film preparation. The microscopic examination showed an acute encephalitis. Ritchie³ inoculated a *rhesus* monkey with two blood-agar cultures in the lumbar region of the spinal cord and the animal died eighteen hours later. The autopsy showed a beginning meningitis, and in film preparations from the surface of the cord and brain, numerous influenza bacilli were found.

VIRULENCE OF THE STRAINS OF BACILLI

We have had the opportunity of studying a large number of strains of influenza bacilli during the past two years, of which four only were found to be virulent for rabbits. It is, perhaps, significant that of these four virulent cultures, three were derived from the cerebrospinal fluid from cases of influenzal meningitis (Cases 4, 7 and 8), and the fourth from the heart's blood at autopsy in a child succumbing to pneumonia. We have endeavored, in many cases at the Babies' Hospital, to obtain the influenza bacillus from the blood of the heart at autopsy, but unsuccessfully, except in the previous case mentioned, until the cases of influenzal meningitis came under observation. In four cases of this infection (5, 6, 7 and 8), the influenza bacillus was obtained from the blood of the heart. The experience of others conforms to our earlier experience. Thus, Wohlwill,¹⁰ who examined many hundreds of autopsies at the Eppendorfer Krankenhaus with this point in view, never secured the bacillus from the blood. Two of the strains of bacilli, which we found to be virulent for rabbits, were also virulent for monkeys. The other two were not tested on the latter animals. One strain of the bacillus obtained from the meninges was found not to be virulent for rabbits and it also was without pathogenetic effect when inoculated into the spinal canal of a monkey. Generally speaking, therefore, high virulence for human beings would appear to indicate high virulence for rabbits and for monkeys also. But this rule, probably, is not free of exceptions. On the other hand, our experience with many strains of the influenza bacillus isolated from the respiratory tract indicates that, in general, the organism possesses virulence for guinea-pigs and mice. One strain only has come into our hands which was devoid of virulence for these animals. All the strains afforded by the cases of meningitis were virulent for small animals. In order to determine this question of virulence, it is imperative that the animal experiments be made immediately after the isolation of the bacilli, since saprophytic cultivation is quickly followed by loss of

10. Wohlwill: München. med. Wehnschr., 1908, 1v, 328.

virulence, the time varying between a few days or weeks and months. Some of our virulent cultures have retained their virulence for rabbits for a period of four months.

SERUM REACTIONS

Agglutination reactions are not satisfactory, and no differentiation of strains is possible by this method.

Opsonins are but slightly more satisfactory. In an immune goat serum, the virulent respiratory strain was phagocyted in as high dilutions as any one of the meningeal strains. Serum from a recovered monkey did not phagocytize the bacilli in dilutions above 1 to 20, and no serum from any human case (respiratory or meningeal) gave any better results.

Complement deviation tests I have found out of the question because of the difficulty of preparing a suitable antigen from these organisms, and since it has not been possible by means of suspensions of washed bacilli or sodium hypochlorite extracts of them to differentiate *Bacillus influenzae* from the Bordet-Gengou bacillus of pertussis, it seemed hopeless to try to differentiate strains by that method.

Protection experiments were made on mice with immune goat serum. This, when given in sufficiently large doses, left the animal alive whether its homologous culture or a meningeal strain were used.

GENERAL CONSIDERATIONS

It would appear from all the facts given that the influenza bacilli isolated from the cerebrospinal fluid from the cases of meningitis are identical with the bacilli commonly obtained from the respiratory tract, and that the chief difference between the bacilli met with in the two situations is one of virulence. This distinction is not fundamental, since equally virulent bacilli are rarely yielded by infections of the respiratory organs.

Since 1903, the number of cases of meningitis due to the influenza bacillus reported in the literature has been increasing. It is significant that in the cases later reported, the influenza bacilli have been found, for the most part, in pure culture, while at an earlier period, mixed infections were more common. This point is probably explained by the imperfect bacteriologic methods originally employed. The frequent finding of the influenza bacillus in cases of endocarditis, purulent arthritis, empyema, appendicitis, peritonitis, meningitis and otitis, as well as their frequent occurrence in the bronchial and nasopharyngeal secretions in cases of clinical influenza, indicates that this organism, like the pneumococcus, is capable of causing inflammations of the serous and mucous membranes anywhere in the body.

A few words should be added on the probable mode of infection of the meninges with the influenza bacillus. It is a well-known fact that the influenza bacilli occur in the nasopharynx in a high percentage of persons exposed to influenza. The upper respiratory tract would appear to be the most frequent portal of entrance into the body for these organisms and to account for their frequent localization in the middle ear, bronchi and lungs. Whether the meninges are infected directly through the lymphatic connections existing between them and the upper nasal mucosa must, for the present, remain an undecided question. The pathogenicity of the influenza bacillus is too slight for monkeys to make it possible to produce in those animals meningitis by inoculating the nasal mucosa. It is of some significance to have learned that after subdural inoculation of the bacilli, the organisms can be recovered from the upper nasal mucosa, suggesting that they are, in part, excreted there. It must, however, be considered that since they also reach the blood they may be secreted from the blood and not directly from the meninges, or that they are contained in the blood in the peripheral circulation, and that a slight injury of the mucosa, inseparable from the making of the cultures, is responsible for their presence in the tubes. That the inoculated animals excrete the bacilli by the nasal mucosa would appear to be shown by the fact that after intravenous injection of the cultures in rabbits, these organisms are met with in the secretions of the mucosa. Normal rabbits and monkeys do not harbor the influenza bacillus in their nasal passages. The bacilli are also excreted by the kidneys in guinea-pigs and rabbits and pure cultures can be recovered from their organs, and usually from the urine as well. Sections of the kidneys showed large numbers of the bacilli lying in the lumen of the tubules, and some within Bowman's capsules. Sections of the lungs showed the bacilli to be present in the capillary blood-vessels of the alveolar walls and in the alveoli themselves. As bearing on the question previously raised as to whether the influenza bacillus can be present in the meninges without setting up inflammation, it should be stated that the surface of the brain and cord of rabbits and guinea-pigs inoculated intravenously or intraperitoneally with cultures regularly yielded pure growths of bacilli, although no lesions or inflammation are associated with their presence.

The bearing of clinical influenza on the origin of influenzal meningitis in human beings is illustrated by the following cases:

In Adams'¹¹ case, the child, which later developed meningitis, had been only slightly ill, but cases of well marked grippe had occurred in the household. No pharyngeal cultures are recorded. In Case 4 of my series, a distinct attack of clinical influenza preceded the meningitis by a week, and cultures from the throat were positive on the second day of

11. Adams: *Arch. Pediat.*, 1907, xxiv, 721.

the meningitis. In Cases 5, 6 and 7, the influenza bacilli were present in the nasopharynx and bronchial secretion on the first days of the meningitis. Davis¹² gives a definite history of "cold" in four of his cases. In such instances as Case 7 and the one reported by Slawyk,¹³ the meningitis must be looked on simply as the terminal effect in a general blood infection with the influenza bacilli. In Hecht's¹⁴ case, the lung was believed to have been the site of the primary lesion. Fraenkel¹⁵ traces one of his cases to a rhinitis, the other to an otitis. Haedke⁵ found influenza bacilli in the pus from the middle ear in his case, and Cohoe⁴ believes that a chronic otitis media, together with trauma, was responsible for the meningeal localization in his case. Cohen¹⁶ believes that his cases were infected through the respiratory tract.

The facts that Pfeiffer¹⁷ had found the influenza bacilli only at the seat of the lesion and not in the circulating blood, even in inoculated animals, and that killed cultures gave rise to symptoms similar to those produced by live bacilli, were responsible for the accepted idea that all the symptoms and complications of influenza are due to the toxins of the bacillus and not to the organism itself. This, in turn, gave rise to a widespread skepticism as to the correctness of positive reports on the finding of *B. influenzae* in the living blood. In Cannon's¹⁸ case, this skepticism was undoubtedly justifiable (1893) and in Letzerisch's¹⁹ (1895) even more so, but Meunier's²⁰ report (1897) of ten cases of bronchopneumonia in young children, in which the bacilli were found during life in blood obtained from the lung eight times and in that from a vein four times, is convincing. It is worth noting that Meunier called attention to the irregular course and fever in such pneumonias, a fact which Holt²¹ has emphasized anew. In 1899, Slawyk¹² published the case of a boy, 9 months old, from whom, during life, the influenza bacillus was grown in pure culture from the cerebrospinal fluid and from the blood of the finger, while at autopsy the bacilli were numerous in sections made from the lungs and were present in pure culture in the pus of an abscess at the left ankle. The interesting points about Slawyk's case are two: the proof that the influenza bacilli are demonstrable in the cerebrospinal fluid during life, and the confirmation by Pfeiffer himself of the bacteriology of the case. With Slawyk's publication, the fact

12. Davis: Proc. Chicago Path. Soc., 1910, viii, 39.

13. Slawyk: Ztschr. f. Hyg., 1899, xxxii, 443.

14. Hecht: Jahrb. f. Kinderh., 1903, lvii, 333.

15. Fraenkel: Ztschr. f. Hyg., 1898, xxvii, 315.

16. Cohen, Ann. de l'Inst. Pasteur, 1909, xxiii, 273.

17. Pfeiffer: Ztschr. f. Hyg., 1893, xiii, 357.

18. Cannon: Virchow's Arch., 1893, cxxxi, 401.

19. Letzerisch: Ztschr. f. klin. Med., 1892, xxi, 274.

20. Meunier: Compt. rend. Soc. de biol., 1897, xxxix, 122.

21. Holt: Jour. Am. Med. Assn., 1910, lv, 1241.

was established that *B. influenza* is capable of invading the blood stream and of causing multiple purulent lesions throughout the human body. Before that date about twenty cases of general infection had been reported, in the majority of which the *B. influenza* has not been found in pure culture. In four of my cases in which it was possible to make a post-mortem blood culture, the bacilli were found in a pure state within one-half to one and a half hours after death. In three of Davis¹² seven cases, influenza bacilli were found pure in the heart's-blood at autopsy. Bentz and Frye²² report a positive blood-culture during life, and Cohen¹⁶ found the bacilli in blood obtained from the tip of the finger before death in two of his cases. In Cohoe's⁴ recovered case, the blood remained sterile. The difficulties encountered in making effectual blood-cultures in young children during life are probably responsible, in part, for the absence of data on this point. It would seem, however, that in the majority of the fatal cases of influenzal meningitis a general blood infection occurs.

Cases of purulent leptomeningitis due to the *B. influenza* have, from time to time, been reported since 1892, when Pfuhl published three cases, in all of which putrefactive bacilli were very numerous. Of the eleven other cases published by Pfuhl,²³ Ghon²⁴ accepts only one, and even that was not due to the influenza bacillus in pure culture. In 1897 Haedke reported one adult case, which he believes to have been caused by the *B. influenza* alone, but which was contaminated after death by putrefactive organisms. In 1898, Fraenkel¹⁵ published two fatal cases in boys of 10 weeks and 9 months of age, respectively. These are the earliest reported cases in young children. Next came Slawyk's¹³ report, the first to place cases of general influenza bacillus infection on a sound bacteriologic basis. In 1900, but one case, that of Meunier²⁵ was reported, and 1901 marked the report of the first recovery from this disease in a 9-year-old boy, observed by Langer.²⁶ Trailescu's⁶ patient, 6 months of age, died. In 1902, four fatal cases were published, of which one (Ghon²⁴) occurred in an adult and did not yield pure cultures, while the others were infants (Ghon, 8 months; Simon,²⁷ 7 months; Dubois,²⁸ 4 months). In Ghon's case, influenza bacilli were found in the lungs as well as in the meningeal pus at autopsy. The year 1903 records five cases with two recoveries,

22. Bentz and Frye: *Woman's Med. Jour.*, 1908, xviii, 73.

23. Pfuhl: *Deutsch. med. Wchnschr.*, 1896, xxii, 82; *Ztschr. f. Hyg.*, 1897, xxvi, 112.

24. Ghon: *Wien. klin. Wchnschr.*, 1902, xv, 667.

25. Meunier: *Compt. rend. Soc. de biol.*, 1900, xlii, 5.

26. Langer: *Jahrb. f. Kinderh.*, 1901, liii, 91.

27. Simon: *Bull. Soc. Anat. de Paris*, 1902, lxxvii, 382.

28. Dubois: *Thèse de Paris*, 1902.

TABLE 1.—CASES OF INFLUENZAL MENINGITIS WITH PURE CULTURES OF *B. INFLUENZÆ*.

No.	Age	Authority	Result	Lumbar Puncture	Autopsy
1	10 weeks.	Fraenkel.	Death.	Not made	<i>B. influenza</i> from meningeal exudate.
2	9 months.	Fraenkel.	Death.	Not made	<i>B. influenza</i> from meningeal exudate.
3	9 months.	Slawyk.	Death.	Cloudy fluid; cultures positive. Also from blood of finger.	<i>B. influenza</i> from meningeal exudate and malleolar abscess.
4	16 months.	Meunier.	Death.	Not made	<i>B. influenza</i> from meningeal and pleural exudate.
5	9 years.	Langer.	Recovery.	Purulent fluid; cultures positive.	
6	6 months.	Trailéscu.	Death.	Transparent, many leukocytes; cultures positive.	
7	6 months.	Ghon.	Death.	Cloudy fluid; cultures positive.	<i>B. influenza</i> from meningeal exudate.
8	8 months.	Simon.	Death.	Turbid fluid; cultures positive.	<i>B. influenza</i> from lungs with coecl.
9	4 months.	Dubois.	Death.	Turbid fluid; cultures positive.	No autopsies.
10	8 months.	Mya.	Death.	Turbid fluid; cultures positive.	No cultures made at autopsy.
11	1 year.	Mya.	Death.	Turbid fluid; cultures positive.	No cultures made at autopsy.
12	9 months.	Mya.	Recovery.	Purulent fluid; cultures positive.	No cultures made at autopsy.
13	9 months.	Caccia.	Recovery.	Pure cultures from the fluid, and from the pus of an otitis media with a Gram-negative coccus.	
14	1 year.	Mya.	Death.	Turbid fluid; cultures positive.	No cultures at autopsy.
15	8 months.	Jündell.	Death.	Purulent fluid; cultures positive.	No autopsies.
16	18 months.	Jündell.	Death.	Not made	Smears positive; cultures failed to grow.
17	12 months.	Cagnetto.	Death.	Not made	Cultures pure from meningeal exudate and spinal fluid.
18	13 months.	Cagnetto.	Death.	Not made	Autopsy.
19	11 months.	Bertini.	Death.	Turbid fluid; cultures positive.	
20	7 years.	Thomasco and Grociski.	Recovery.	No details given; cultures pure.	
21	4 years.	Cattaneo.	Death.	Purulent fluid; cultures pure.	Cultures from minigeal pus and middle ears.
22	10 months.	Douglas.	Death.	Yellowish fluid; many polymorphs; positive cultures.	At autopsy, pure influenza cultures from hip-joint, pus and spleen.
23	10 months.	Dudgeon and Adams.	Death.	Turbid fluid; cultures positive.	No autopsies.
24	5 years.	Adams.	Death.	Quite turbid; deposit of pus; pure.	
25	4 years.	Springg.	Death.	Made after death. Cloudy fluid; cultures pure.	At autopsy, cultures pure from brain pus, with streptococci in blood.
26	21 months.	Bontz and Frye.	Death.	Cloudy fluid; cultures pure; blood culture pure.	At autopsy, no cultures made.
27	4 months.	Cohen.	Death.	Turbid fluid; cultures pure.	No autopsies.
28	1 year.	Cohen.	Death.	Turbid fluid; cultures pure, and also from blood of finger.	No autopsies.
29	8 years.	Cohen.	Death.	Slightly turbid fluid; cultures pure; also from blood of finger, pus in wrist-joint and fluid from lung.	
30	Adult.	Cohoe.	Recovery.	Very slightly turbid fluid; cultures positive.	
31	9 days.	Davis.	Death.	Not made	At autopsy, pure cultures from meningeal pus and peritoneum.
32	12 days.	Davis.	Death.	Not made	No autopsies.

TABLE 1.—CONTINUED

33	6 months.	Agar and Avery.	Death.	Turbid fluid; cultures positive.....	At autopsy, cultures pure.
34	19 months.	Ritchie.	Death.	Faintly opalescent fluid; second more turbid; cul- tures positive.....	No autopsy.
35	Infant.	Ritchie.	Death.	Turbid fluid; cultures positive.....	No autopsy.
36	13 months.	Davis.	Death.	Turbid fluid; cultures positive.....	At autopsy, cultures from meningeal pus, heart's blood and pericardial fluid.
37	7 months.	Davis.	Death.	Many polymorphs in fluid; cultures positive.....	At autopsy, cultures from meningeal pus and heart's blood.
38	Infant.	Simon and Ainc.	Death.	No details given, but cultures reported pure in all....	Not stated.
39	Infant.	Simon and Ainc.	Death.	No details given, but cultures reported pure in all....	Not stated.
40	Infant.	Simon and Ainc.	Death.	No details given, but cultures reported pure in all....	Not stated.
41	Infant.	Simon and Ainc.	Death.	No details given, but cultures reported pure in all....	Not stated.
42	Child.	Simon and Ainc.	Death.	No details given, but cultures reported pure in all....	Not stated.
43	3 years.	Wollstein.	Death.	Very turbid fluid; cultures pure.....	No autopsy.
44	2 years.	Wollstein.	Death.	Very turbid fluid; cultures pure.....	No autopsy.
45	3 3/4 years.	Wollstein.	Death.	Purulent fluid; cultures pure.....	No autopsy.
46	6 months.	Wollstein.	Death.	Turbid fluid; cultures pure.....	No autopsy. p. m.
47	2 years.	Wollstein.	Death.	Turbid fluid; cultures pure; later, thick pus.....	Culture from heart pure 1 1/2 hours
48	8 months.	Wollstein.	Death.	Turbid fluid; cultures pure.....	Culture from heart pure 1 hour p. m. At autopsy, culture pure from meningeal pus, elbow- joint and heart's blood with streptococci in the lungs.
49	5 months.	Wollstein.	Death.	Purulent fluid; cultures pure.....	No autopsy. p. m.

TABLE 2.—CASES DUE TO B. INFLUENZÆ WITH OTHER BACTERIA

No.	Age	Authority	Result	Lumbar Puncture	Autopsy
1	Adult.	Högerstedt.	Death.	Not made	Contaminating bacteria not named at autopsy; cultures almost pure.
2	Adult.	Fühl.	Death.	Turbid fluid; no cultures.	At autopsy, cultures mixed with streptococci and pneumococci.
3	Adult.	Haedke.	Death.	Clear; later, turbid; no cultures.	At autopsy, cultures mixed with putrefactive bacteria.
4	5 months.	Punker.	Death.	Not made	At autopsy, cultures mixed with staphylococci.
5	Adult.	Ghon.	Death.	Purulent fluid; cultures mixed with Gram-negative diplococci.	At autopsy, cultures mixed with streptococci.
6	2 years.	Hecht.	Death.	No made	At autopsy, cultures mixed with pneumococci.
7	6 years.	Retini.	Death.	Not made	At autopsy, cultures mixed with saprophytes.
8	1 year.	Davis.	Death.	Films characteristic; turbid fluid; cultures failed to grow.	At autopsy, cultures mixed with streptococci.
9	6 months.				

TABLE 3.—DOUBTFUL CASES

No.	Age	Authority	Result	Lumbar Puncture	Autopsy
1	Adult.	Testevin.	Death.	Fluid with much pus	At autopsy (of spine only), diplo-bacilli of influenza grew on serum agar.
2	3 years.	Nuttall and Hunter.	Death.	Fluid clear; ill two months; cultures of meningococci, and, in smears, bacilli which authors are "inclined to regard" as influenza.	
3	4 months.	Nuttall and Hunter.	Death.	Fluid clear; ill five weeks; cultures of meningococci and, in smears, bacilli which authors are "inclined to regard" as influenza.	
4	1 year.	Nuttall and Hunter.	Death.	No details given.	
5		Morosov.	Death.	Very turbid fluid; smears positive; no cultures.	<i>B. influenzae</i> alone, but no details given.
6	11 months.	Charles.	Death.	Slightly turbid fluid; smears positive; streptothrix grew, but only in one generation.	No autopsy.
7	5 months.	Ritchie.	Death.	Turbid fluid; films characteristic; cultures not studied.	No autopsy.
8	6 months.	Davis.	Death.		

both in babies 9 months of age, observed by Caccia²⁹ and by Mya,³⁰ the latter publishing three other cases. In the following year, Jündell³¹ and Cagnetto³² each reported two pure cases and Bertini³³ one, all in children between the ages of 8 and 18 months. In 1904 also, a fourth recovered case, in a boy 7 years old, came under the observation of Thomesco and Gracoski.³⁴ Cattaneo³⁵ in 1905 reports a fatal case in a 4-year-old boy. During 1907, cases were reported by Douglas³⁶ (10 months); Dudgeon and Adams³⁷ (10 months); Adams¹¹ (5 years); Sprigg³⁸ (4 years); and Carles³⁹ (11 months), but in the last case no cultures are recorded, only smears from the abundant fibrino-purulent deposit of the lumbar puncture fluid. Only one case appeared in 1908, reported by Bentz and Frye.²² In 1909 Cohoe⁴ placed on record a recovery in an adult, and Davis,⁴⁰ the two youngest patients known, twins aged 9 and 12 days, respectively. Cohen's¹⁶ patients were 4, 8 and 12 months old, but he chooses to look on the bacillus isolated from his cases as distinct from the *B. influenza* because of its greater virulence and the difference in its serum reactions when compared with a strain obtained from Pfeiffer. During 1910, Davis¹² reported five additional fatal cases, in infants from 6 to 13 months of age, two being pure. Agar's publication records Case 1 of this paper. Ritchie's³ description of the "influenza-like" bacillus found in his three cases shows that very many long filaments were present, even in young cultures. The fact that after some months of cultivation on blood-agar the bacillus grew on ordinary agar, on which subculturing was possible for some weeks, would seem to take it out of the class of influenza bacilli. Simon and Aine⁴¹ tell of five cases, four of them in infants. Cases of meningitis, in which influenza bacilli were found in addition to other organisms have been reported by Högerstedt⁴² in an adult, Peucker⁴³ in a 5-months-old baby, Hecht¹⁴ in a child of 2 years, and Bertini³³ in a 6-year-old boy. One of Davis'¹² cases was contaminated by saprophytes, and in another streptococci were present with the influenza bacilli. Nuttall and Hunter,⁴⁴ while studying the meningo-

29. Caccia: Ref'd to in Centralt. f. Bakteriöl., 1904, xxxv, 106.

30. Mya: Gaz. d. Osp., 1903, xxiv, 268; Riv. clin. Pediat., 1903, xxiii, 465.

31. Jündell: Jahrb. f. Kinderh., 1904, lix, 777.

32. Cagnetto: Cited by Ritchie, Jour. Path. and Bacteriol., 1910, xiv, 615.

33. Bertini: Riv. clin. Pediat., 1904, ii, 673.

34. Thomesco and Gracoski: Rév. neurol., 1905, xiii, 44.

35. Cattaneo: Baumgarten's Jahresb., 1905, xxi, 289.

36. Douglas: Lancet, London, 1907, i, 86.

37. Dudgeon and Adams: Lancet, London, 1907, ii, 684.

38. Sprigg: Am. Jour. Obst., 1907, lvi, 467.

39. Carles: Jour. de med. de Bordeaux, 1907, xxxvii, 106.

40. Davis: Arch. Int. Med., 1909, iv, 323.

41. Simon and Aine: Semaine Méd., 1910, xxx, 513.

42. Högerstedt: St. Petersburg. med. Wehnschr., 1895, xii, 123.

43. Peucker: Prag. med. Wehnschr., 1901, xxvi, 153.

44. Nuttall and Hunter: Lancet, London, 1901, i, 1524.

coccus, came on three cases of meningitis in a late stage, in which the clear cerebrospinal fluid contained the diplococci and also bacilli which, from their morphology and staining, they were inclined to regard as influenza bacilli. It is obvious that such cases cannot be accepted without cultural isolation of the bacilli. Morosow's case⁴⁵ is given so meagerly that it is difficult to judge of its authenticity. Testevin⁴⁶ made a lumbar puncture in an adult case of meningitis and spinal caries, obtaining purulent fluid with an "infected odor." A partial autopsy only was performed, and from the meningeal pus the "diplobacilli of grippe" grew on serum-agar, making this case more than doubtful. All the reported cases are tabulated below.

The great preponderance of cases of influenzal meningitis among young infants and its very high mortality are very striking, as is the opportunity which lumbar puncture gives for early and correct differential diagnosis in this disease. Thus, since Slawyk's positive case in 1899, there have been forty-four cases of pure influenzal meningitis reported, and in thirty-three of these the diagnosis was made from cultures of the cerebrospinal fluid before death. In all there are forty-nine cases of pure and nine cases of mixed influenzal meningitis on record, of which only five were adult subjects, and twenty-eight were under 1 year of age. Five recoveries occurred, all among the pure cases; one patient was an adult, one was 9 years old, another 7 years, and two were 9 months of age.

45. Morosow: St. Petersburg. med. Wehnschr., 1904, xxi, No. 6, 40.

46. Testevin: Dauphiné Méd., 1897, xxi, 49.

AMAUROTIC FAMILY IDIOCY *

ISAAC A. ABT, M.D.

CHICAGO

During the year a case of amaurotic family idiocy has come under my observation in my service at the Michael Reese Hospital, Chicago. I was enabled to study the case clinically and also was fortunate enough to secure a complete autopsy. Notwithstanding the fact that numerous cases have been reported by American and European writers, the case is thought to be of sufficient interest to warrant publication.

B. Sachs¹ was the first to use the designation "amaurotic family idiocy," applied to an interesting family disease occurring in infancy, characterized by an entire lack of mental development, by a progressive weakness of all the muscles of the body, and by rapidly developing blindness, associated with typical changes in the macula lutea. The disease is, according to Sachs, generally fatal, the patients dying, as a rule, in a condition of complete marasmus before the end of the second year of life.

REPORT OF CASE

History.—The patient was a male child, 18 months old, born of Jewish parents, and was admitted on Sept. 18, 1909. The birth was uneventful; no forceps were used, and the delivery was easy. The child weighed 10 pounds at birth. The eruption of the teeth came late, beginning at the tenth month. The child progressed normally up to the eighth month of life. Until 1 year old the baby had mother's milk; after that, cow's milk, soup, potatoes, and almost everything. This diet seemed to agree with the baby, and he increased in weight.

History of Illness.—At about 8 months of age, the child began to show signs of listlessness. He moved his limbs very little, the movements being aimless. Paralysis gradually developed, up to the time of examination. The mother stated that the child saw little, or not at all. At the time of examination he could not sit up or move his legs. He could move his hands only a little. For the past ten days he had had difficulty in swallowing. The eyeballs did not act in unison; they rolled from side to side, and also moved outward and upward. This motion was almost constant. Loud sounds, such as slamming of a door, or slight noises, threw him into convulsions, which lasted for several seconds. The appetite was normal; digestion good; bowels normal. For the past two weeks the child had cried more than usual; appeared to be losing in weight. He had had for the past six months, at varying intervals, choking spells. He had suffered from none of the infectious diseases. The only acute illness was a gastro-enteritis two months previous, not severe in character. It lasted about a week.

Family History.—The first child died, in exactly the same condition from which our patient is suffering, at 18 months of age. The second child was 4 years

* Read in the Section on Diseases of Children of the American Medical Association, at the Sixty-first Annual Session, held at St. Louis, June, 1910.

1. Osler's Medicine, 1910, p. 868.

old and well. The patient was the third child. The mother and father were well, except that father had attacks of asthma. The grandparents' history was negative.

Physical Examination.—General appearance was that of a large child, with a prominent head. Saliva drooled from the mouth. The expression was vacant. The eyes rolled in all directions.

Head: The scalp was negative. Dimensions of head were somewhat larger than normal; the sutures and the fontanelles were closed.

Eyes: The pupils were equal, reacted sluggishly to light, and showed a nystagmus, but also an outward and upward movement, which has already been referred to.

The examination of ears, mouth and pharynx, neck, chest, heart and lungs was negative.

Abdomen: Liver was normal in size and position. Spleen was palpable; otherwise negative.



Fig. 1. Ophthalmoscopic picture of eye ground in a case of amaurotic family idiocy.

Extremities: Arms appeared to be spastic, with a distinct wrist-drop and an outward rotation of the forearms was noted. The arms occasionally showed a flaccid paresis. The spastic and flaccid conditions seemed to alternate. The legs also showed a spastic paralysis and were in the extended position, with a typical foot-drop.

Reflexes: Eyes reacted to light sluggishly. Abdominal reflexes were slow. Knee reflexes were decreased. Babinski sign was present on right foot, but not on left.

Sensations: Tactile and pain sensations seemed to be exaggerated in legs, but not in arms.

Genitals: Right testicle was only partially descended.

Ophthalmoscopic Examination: Dr. Mortimer Frank reported the pathognomonic condition in retina, which was as follows: "About the macula lutea (Fig. 1) is a nebulous area, grayish-white in color, slightly raised above the surface of the



Fig. 2.—Section of posterior half of the eye showing the region about the macula.

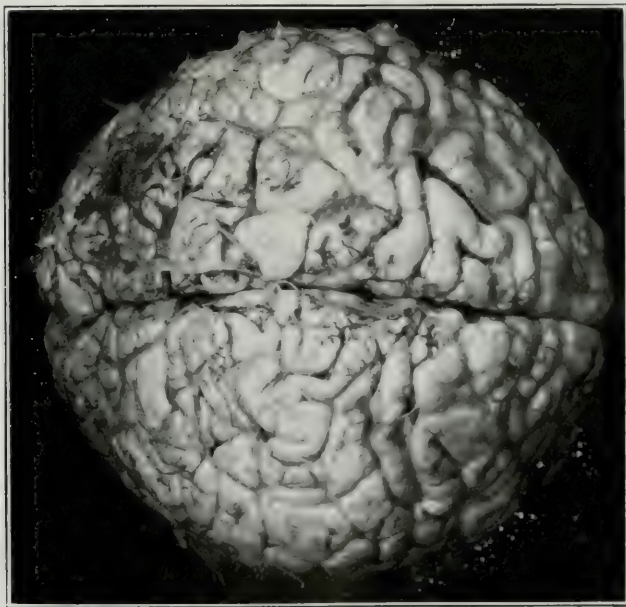


Fig. 3.—Convex surface of brain, case of amaurotic family idiocy. No gross lesion.

retina, and about two to three times the size of the optic disc. The patch is oval in shape, with the major axis horizontal. In the center, coinciding with the fovea centralis, but larger, is a dark red, or cherry-colored spot, clear-cut in outline."

Two spinal punctures were made. The fluid was more than normal in amount; it exuded under high pressure, but was negative as to its microscopic and chemical findings.

The blood, feces and urine were negative.

Course of Disease.—The child lived for twenty-one days after admission. Temperature and pulse were practically normal throughout the disease, with the exception of last few days of life, when the child's temperature rose as high as 106 F.; pulse rapid, running up to 160. Abdominal reflexes appeared to be absent on some days, though on other days they were highly exaggerated. The same was noted of knee reflexes. Babinski sign was present on both sides at

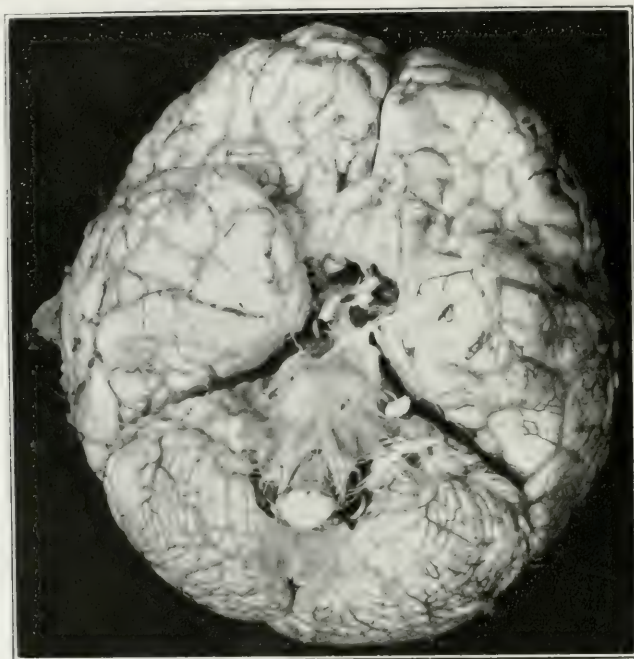


Fig. 4. Basal surface of brain, case of amaurotic family idiocy. No gross lesion.

times, and occasionally entirely absent. The arms occasionally showed a catatonic state. Clonic convulsions were noted quite frequently, especially when slight noises were made. Choking spells occurred while the child was being fed. Drooling of saliva was almost constant. The child could not support the head. During the last few days of the disease the nystagmus ceased, but a constant outward and upward movement of eyeballs was noted and all the reflexes were exaggerated.

Summary of Clinical Symptoms and Physical Findings

1. Death of two children from this disease in the same family, the patient being the second.
2. Insidious onset, inability to support the head, gradual development of muscular weakness, going on to alternating flaccid and spastic paralysis.
3. Gradual development of blindness.

4. Pathognomonic sign in the macula lutea (cherry spot).
5. Constant and irregular nystagmus.
6. Alternating absence and presence of reflexes.
7. Hyperacusis (increased sensitiveness to sounds), throwing the child into convulsions.

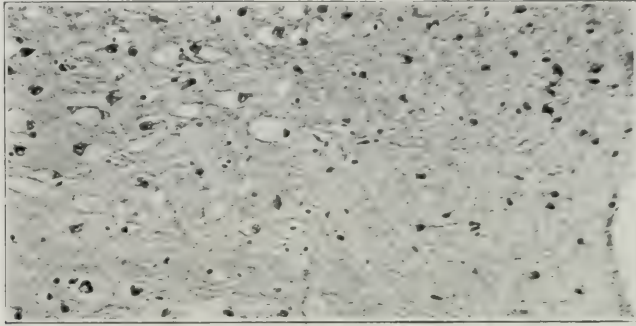


Fig. 5.—Cerebral cortex, parietal area, showing absence of external polymorphous cell layer.

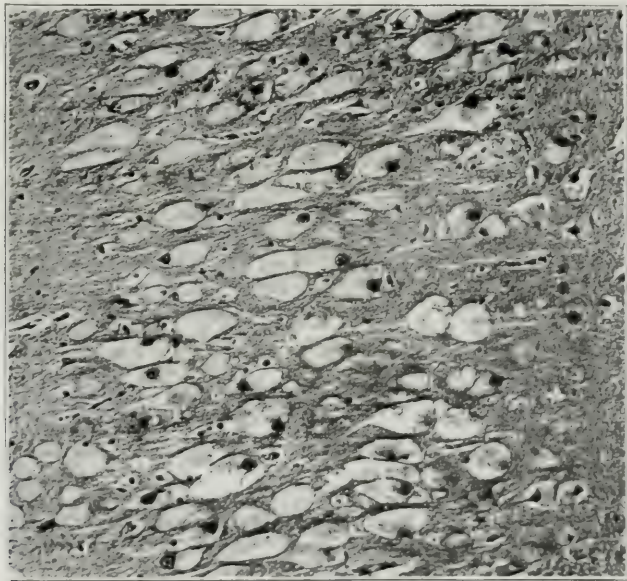


Fig. 6.—Cells in cortical region of hippocampus major. Loss of tigroid substance; eccentrically placed nucleus.

8. Impaired deglutition and choking spells.
9. Digestion normal.
10. Constant drooling of saliva.
11. Last stage of the disease, characterized by loss in fat and weight and marked asthenia.

Pathologic Report on Eyes. The pathologic examination of the eyes was made by Dr. Mortimer Frank, whose report follows: The specimens were fixed in formaldehyd solution, and cut in an anterior and posterior half, so as to show the area surrounding the macula. The globes before cutting measured 18 mm. from side to side, 17 mm. from before backward, and 17 mm. from above downward. Except for slight corneal abrasions, nothing unusual was found in the anterior halves. The posterior halves presented in the region of the macula a grayish zone, 2 mm. by 1 mm., somewhat elliptical in shape, with the ends pointed, in the center of which was a dark-brown depression about the size of a pin-point, corresponding to the fovea centralis. This area corresponding to the striking ophthalmoscopic picture seen in the living eye. The disks were almost white, with central arteries crossing them. One of the halves was mounted in glycerin-formaldehyd jelly and the other sectioned serially (Fig. 2). A distinct hole, as described by Parsons, was seen, but no edema. Briefly, the changes in the eye

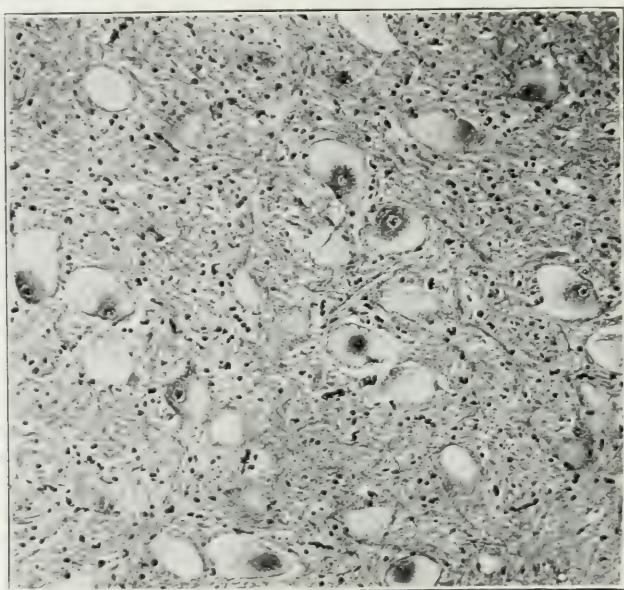


Fig. 7.—Cells of Clark's column. Tigrolysis in some cells; complete loss of tigroid substance in other cells.

were of a degenerative type, affecting chiefly the ganglion cells of the retina, but in a greater degree those in the macula. The optic nerve likewise showed the same degenerative changes.

General Pathologic Report.—The brain and cord were referred by Dr. James W. Jobling, pathologist of Michael Reese Hospital, to Dr. M. G. Schlapp, instructor in neuro-pathology at Cornell University Medical College, who has very kindly furnished the pathologic report. The photographs were taken by Dr. Jaques.

A striking feature about the lesion found in amaurotic family idiocy is the fact that all the nerve cells in the cerebrospinal nervous system are involved. The most distinctive changes in this case are those found in the cerebral cortex (Fig. 5) affecting equally the different areas, but the

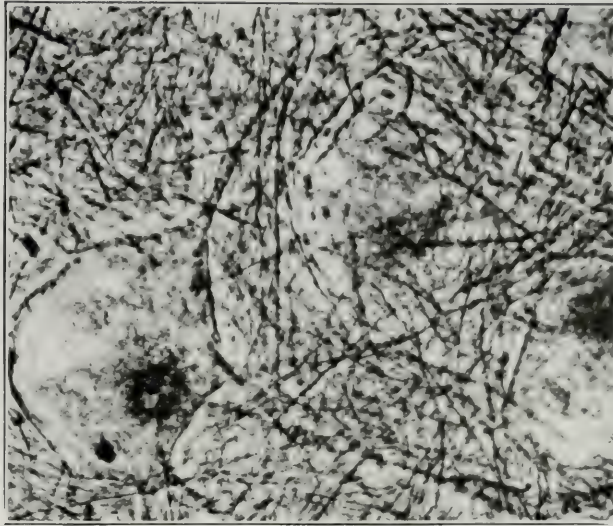


Fig. 8.—Section showing cells in anterior horn of spinal column (Bielschowsky's stain). Destruction of intracellular fibrils. The peripheral fibrils still existing and continuing into the dendrites.

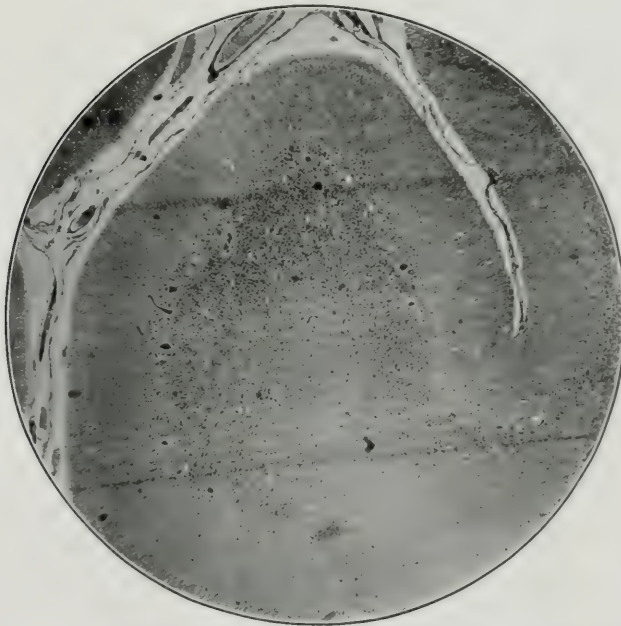


Fig. 9.—Cerebellar cortex: granule cells decreased in numbers.

same changes are also to be seen in the cord, especially involving the cells of Clark's column (Fig. 7).

It is impossible to differentiate the several layers of the cerebral cortex, partly on account of the disappearance of many cells, and partly because of the changed appearance of the cells remaining (Fig. 6). The cells of this region, regardless of variety, show a marked swelling of the cell body, almost entire loss of the tigroid substance, and a nucleus which occupies an eccentric position. The disappearance of the tigroid substance seems to have taken place first at the periphery of the cell, and then progressed toward the nucleus. In quite a number the only tigroid substance remaining is in the form of a mantle surrounding the nucleus,

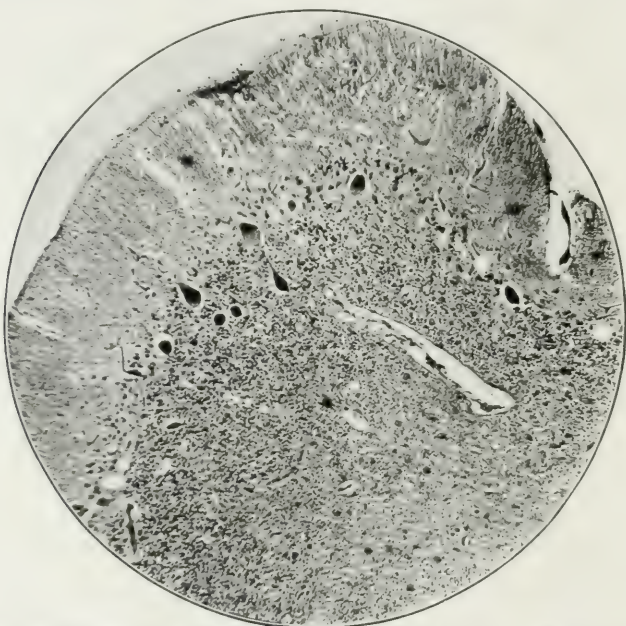


Fig. 10. Cerebellar cortex (hematoxylin and acid rubin). Nuclei of Purkinje cells retain central position. Tigroid substance beginning to disappear, but found around nuclei.

and in the larger portion of these cells the nucleus is apical in its relation to the cell body, and the tigroid substance, when present, extends into the adjoining dendrites, which also appear swollen. This loss of tigroid substance is confined wholly to the cell body; there does not appear to be any diminution in the dendrites. The marked swelling of the cells, with the loss of tigroid substance, causes the cells to stand out distinctly as light areas, and to assume a balloon appearance. In some cells the nuclei do not present round, well-formed bodies, but are broken up into small fragments, resembling the chromatin substance of the nucleoli. Distinct vacuoles are present in the periphery of some of the cells.

By Bielschowsky's fibril stain it is apparent (Fig. 8) that the intracellular fibrils are being destroyed, and that the fibrils lying at the periphery of the cell body are much better preserved, as are also the continuation of these peripheral fibrils into the dendrites. Excepting for the swollen condition of the dendrites, this stain also brings out the fact that the abnormal changes are confined almost wholly to the cells, the cell processes appearing practically normal.

The changes are least marked in the cerebellum (Figs. 9 and 10) and in the postspinal ganglia. In the cerebellum the layer of granule cells is present, but the number of these cells seems to be diminished. The Purkinje cells show some change, but they are not as marked as are the

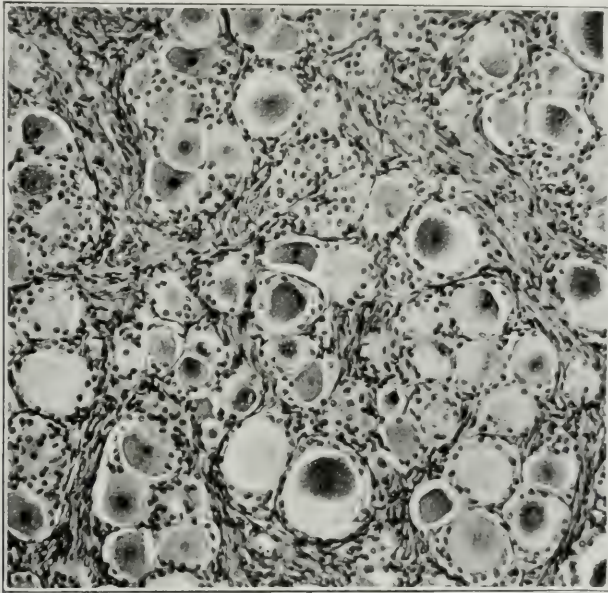


Fig. 11. — Spinal ganglion. Disappearance of tigroid substance. Around nucleus tigroid substance left.

changes in the cerebral cells or nerve cells in other parts of the central nervous system. The nuclei in the majority of these cells retain their central position and stain intensely with hematoxylin. The tigroid substance is beginning to disappear at the periphery of the cells, but is still found around the nuclei.

The nerve cells of the cord (Figs. 11 and 12) show practically the same changes, though to a somewhat less degree, as those already described as occurring in the cells of the brain. They are markedly swollen, and the tigroid substance and intracellular fibrils have in most instances almost entirely disappeared.

We have, therefore, the following marked changes in the cell, recognized by Nissl: hematoxylin, eosin, Van Giesen, and other cell stains:

1. Swollen condition of cell body.
2. Complete or partial loss of tigroid substance. If any tigroid granules are present, they are to be found around the nucleus.
3. Eccentric position of nucleus with various abnormal appearances; irregular outlines; some nuclei intensely stained with hematoxylin, others not; disintegration of nucleolus.
4. Pericellular lymph-spaces much distended.
5. In advanced stages of degeneration a complete disintegration of remaining substance of cell body.

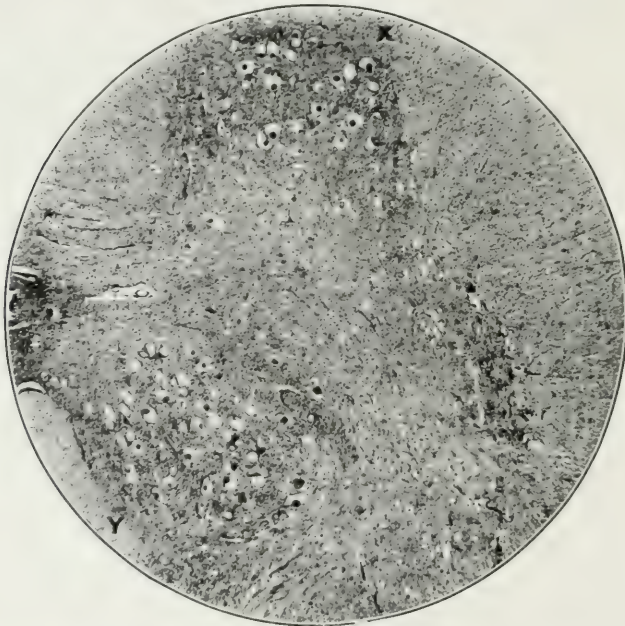


Fig. 12.—Anterior horn (x) of spinal cord and Clark's column (y). Cells swollen. Tigroid substance and intracellular fibers disappear.

CLASSIFICATION

Two forms of amaurotic family idiocy have been differentiated:²

1. *Infantile Form*.—The course, as has been frequently described, is characterized by the occurrence of the disease some time during the third or fourth month of life, though the children are born healthy and remain normal until overtaken. Syphilis and other constitutional diseases of the parents are absent. As a rule, several children in the same family are affected. Many of the children come from families having neuropathic

2. Vogt: Arch. f. Kinderh., li, 1.

or psychopathic taint, and at the same time it may be said that the majority of cases occur in Jewish children. According to the statistics of Heverock,³ who collected reports of eighty-six cases, sixty-one occurred among Jewish children, seven among Christian children, and in seventeen the race and religion were not noted.

The onset of the disease is usually gradual and only after days or weeks of ill-defined symptoms is the disease recognized. First of all, the patients seem to grow less lively; they show lassitude; manifest little or no interest in their surroundings, and desire to sleep. It is also noted that about this time the children do not follow objects with their eyes. Later on, when the physician is called, he suspects that the child is blind or has a seriously defective vision, and the ophthalmoscopic examination shows a light macula with a red punctiform center, and with atrophy of the optic nerve. The changes in the macula precede the pupillary changes. If the child is seen early and is not blind, he soon becomes so. Nystagmus and deviation of the eyes is a frequent occurrence. Hyperacusis, deafness and loss of smell sense are frequently present. The pupils are, as a rule, asymmetrical, and only rarely do they fail to react. Increased salivary secretion with profuse discharge and wide open mouth are frequently reported. The reflexes, particularly the patellar, may be increased, or absent, or unchanged. Frequently the head cannot be held erect and falls on the breast. As the disease progresses, pronounced weakness of the extremities occurs, the child lies motionless, the musculature is relaxed and naturally loss of weight occurs.

Little by little a general paralysis sets in, which is most often flaccid, though occasionally spastic. Later on rigidity of the extremities occurs. Mentally, the children deteriorate and eventually show no reaction. They lose more and more in weight and the disease terminates in marasmus.

2. *Juvenile Form*.—A juvenile form is also described. Clinical observations would indicate that the disease described by Sachs and Fay may occur in juvenile age. Cases of this kind have been described by Higier and Freud and more detailed descriptions by Spielmeyer and H. Vogt.

While Sachs does not deny the close resemblance between these two forms of the disease, he does not consider them identical. The juvenile form, although associated with blindness, does not show the macular changes which are pathognomonic in the infantile form.

100 State Street.

3. Heverock: Neurol. Centralbl., 1904, p. 948.

ATYPICAL SCARLET FEVER*

CHARLES GILMORE KERLEY, M.D.

NEW YORK

Among the diseases of children which we are called on to treat there is none other which may present itself in such peculiar and unusual ways as scarlet fever. This, together with the fact that we have no positive means of proving our case, either clinically or bacteriologically, renders scarlet fever a disease difficult and in some instances impossible of diagnosis.

Thus we see cases of evident scarlet fever showing the typical rash, throat, glands and temperature reaction, and yet the child never desquamates. Is desquamation necessary? A boy 4 years old became ill with what I diagnosed and considered a typical moderately severe scarlet fever. We kept up quarantine for seven weeks, watching for the desquamation which never came in spite of a very intense rash, and which did not appear later.

During a visitation of scarlet fever to a family, four children were attacked. Dr. S. Finley Bell had treated the two other members of the family at Englewood, a suburb of New York; a trained nurse caring for the children contracted the disease and died. Later a girl 6 years old died with the disease. At one of my visits to one of the children who had been sent to New York City and later developed the disease, a member of the family called my attention to the arms of the laundress, which were slightly reddened. It was Monday morning and she was washing. There was no temperature, a normal throat, no rash elsewhere and the girl felt well and was annoyed that she should be disturbed with her work. The redness of the arms disappeared after the completion of the washing and nothing more was thought of the woman until she was found to be desquamating profusely on the hands and feet with slight desquamation over the body generally. She was visited by an expert from the health department and sent to the Willard Parker Hospital where she required two weeks to complete the desquamation. Here was a case in which a most careful search failed to reveal anything approaching conclusive evidence of scarlet fever and yet the woman had the disease at the time.

The father of two of my young patients came into my office and asked me to look at his hands which were desquamating freely, as were also his feet. He said his wife was in the same condition and wanted to know if they had scarlet fever. Two weeks previously they had both had an itching of the skin which they had ascribed to some dietetic error. The

*Read in the Section on Diseases of Children of the American Medical Association, at the Sixty-first Annual Session, held at St. Louis, June, 1910.

mother was seen and was desquamating. I have seen hundreds of children desquamate with scarlet fever and this desquamating was in all respects similar. We isolated the two children who had previously been in daily contact with them and neither became ill, and no other case could be traced to the couple.

A boy 14 years old became ill with tonsillitis and an indefinite rash which was diagnosed as urticaria. After two days the rash had disappeared. The boy recovered from the illness, mixed with other members of the family, which consisted of the father and mother and three other children, two younger than the boy. Not one of them contracted scarlet fever. The boy circulated among his fellows. To my dismay, after three weeks from the beginning of the illness desquamation began on the feet and hands. The desquamation was very free, requiring about three weeks to complete. Did this boy have scarlet fever?

A girl 3 years of age developed a typical scarlet fever rash without temperature and with a normal throat. The rash was characteristic and, since a younger child was in the house, a vigorous quarantine was established. The rash subsided and the skin was clear in five days. At the end of the second week, a very general desquamation of the entire body appeared including the palms of the hands and the soles of the feet. The desquamation was slow, requiring nearly three weeks for completion.

A boy 2 years of age developed a rash somewhat resembling German measles. He had a congested throat and fever. There were other cases of scarlet fever in the apartment. This boy had been exposed and there were other children in the family. An expert from the health department diagnosed the case as German measles and dismissed it. I was not satisfied with the diagnosis and kept the child in quarantine because of the angina in association with a nondescript rash. In three weeks from the onset desquamation began and ran the usual course.

A boy 18 months old, an inmate of a New York institution for children, was noticed, when he was stripped for weighing, to have a typical scarlet fever eruption over the outer left thigh. There was no eruption elsewhere at any time. I was called and confirmed the nurse's diagnosis as to the nature of the rash. The boy had a temperature of 102° F. at the time. He was one of an epidemic of 109 cases. He was very slightly ill. The rash faded rapidly and, of all the 109 cases, he probably desquamated the most freely, the epidermis coming off in large masses.

A girl 5 years of age developed scarlet fever; the attack was moderately severe. Everything occurred on time, the desquamation being completed at the end of the fifth week. Two weeks later the child went to the sea-shore and while walking barefooted on the sand a trained nurse noticed that she was desquamating on the feet. This was reported to the hotel office. The child returned home and went through a second desqua-

mation, requiring about twenty days. One other case of second desquamation has come under my observation.

I was called by Dr. Rodman of New York City to see a boy 6 years of age, ill with scarlet fever. The child was desperately ill, a typical severe case with rash, angina, adenitis, high temperature and prostration. The child died a few days later. On getting the history I was told by the physician that this was the second attack, the patient having recovered from a previous attack three months before, and that there was no doubt as to the previous illness. The mother, an intelligent woman, described in detail the character and duration of the desquamation, substantiating the physician's opinion.

Every year we see cases of acute nephritis following undiagnosed scarlet fever. Usually the rash is very slight, not characteristic and thought to be indigestion, the child being ill but a day or two if at all.

I might recite many other instances of unusual manifestations of the disease under consideration. Enough has been said to bear out the opening statement that scarlet fever is a disease which may manifest itself in peculiar and unusual ways.

A fairly large experience covering hospital and private work for twenty-two years, has led me to believe:

1. In many cases, scarlet fever is never recognized.
2. Scarlet fever is a disease of direct infection; it is rarely carried by a second person or object.
3. The most contagious period is early in the disease during the period of angina, rash, and temperature.
4. The dangers of transmitting the disease during the desquamation period is much exaggerated.
5. Wrongly diagnosed and unsuspected cases are the great transmitters of the disease.
6. During a scarlet fever epidemic, every suspect must be quarantined until he gives reasonable proof of innocence.
7. The most constant symptom is the angina, a deep general congestion of the fauces; but this may fail.
8. In its symptomatology scarlet fever is the most inconstant of the exanthemata.
9. In its severity there are the widest possibilities. I have seen children die in thirty-six hours from the onset, and I have had cases escape my recognition when I was looking for them.
10. It is a disease in which some definite diagnostic sign is greatly to be desired.

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PROGRESS IN PEDIATRICS

ANATOMY AND PHYSIOLOGY

Contributions to the Study of Cutaneous Reactions

(Hans Schmidt. *Arch. f. Kinderh.*, 1910, lvi, Nos. 4-6)

The author investigated the action of different food substances when applied to the skin as in a Pirquet test. The materials used were: 1. A substance composed of 40 per cent. meat extract, 20 per cent. egg albumen, 6.9 per cent. glycerin, salt and water. 2. A milk rich in fat, predigested with trypsin. The tests were made on 100 children suffering with different diseases. The reaction when positive resembled that of a positive Pirquet test. In 40 per cent. the reactions were positive. The influence of the different diseases on the determination of the reaction was not marked; the largest number of positive reactions was found in the case of functional neurosis and in the arthritic diathesis. The influence of age was, however, very marked, as shown by 20 per cent. of positive reactions in infancy as compared with 77 per cent. in patients over 10 years of age. It was found that a large number of those giving positive reactions had had several infectious diseases. Any direct relation between special diseases and positive reactions was not found.

G. L. MEIGS.

Salt Fever and Excretion of Chlorin in Infancy

(Ragner Freiburger. *Arch. f. Kinderh.*, 1910, lvi, Nos. 1-3, p. 17)

The author gave eighty-three injections of salt solution to twenty children; a rise of temperature was noted after twenty-six injections in twelve of the children. In eight there was never any rise in temperature. His conclusions are that fever is often caused by the subcutaneous injection of salt solution, but this is very variable and uncertain; children suffering with nutritional disturbances more often show a rise in temperature than do normal children; the reaction seems to depend on the amount of salt given, 60 c.c. causing a reaction in 33 per cent., 10 c.c. in only 20 per cent.; there is no diminution in reaction caused by a repetition of the injections. Experiments were also made to determine whether there was a rise in temperature after the oral administration of salt; fifty-four experiments were made on eleven children; a reaction was present after eight experiments. Freiburger disagrees with the theory that the fever is caused by an action on the heat-regulating apparatus of the central nervous system, but thinks it probable that it may be caused by a reaction to some destructive change in the body cells caused by the salt. As to the excretion of chlorin in infancy, his conclusions are that salt injected subcutaneously is more slowly excreted than that taken by mouth; the excretion of salt is diminished in children suffering with nutritional disturbances or with the exudative diathesis.

G. L. MEIGS.

METABOLISM AND NUTRITION

The Mineral Metabolism of a Healthy Breast-Fed Baby

(Tobler and Noll. *Monatschr. f. Kinderh.*, 1910, ix, No. 4, p. 210)

In a six days' metabolism experiment on a healthy baby aged 2½ months, Tobler and Noll found that retention of the various salts in the body was as

follows: K_2O , 50.27 per cent.; Na_2O , 92.64 per cent.; CaO , 22.3 per cent.; Cl_2 , 15.34 per cent.; P_2O_5 , 56.51 per cent., and SO_3 , 41.29 per cent.

Fritz B. Talbot.

Casein Milk in the Nutrition of Infants

(W. Birk. *Monatschr. f. Kinderh.*, 1910, ix, No. 3, p. 140)

Birk fed thirty acutely or chronically sick babies with "Eiweiss-milch" (casein milk of Finkelstein and Meyer), which contains a low percentage of sugar and salts and a high percentage of casein. Five of the babies died soon or immediately after starting the use of the milk. A sixth was made worse by the food. Improvement in a child comes in the following way: first, a typical alkaline soap stool appears in place of the watery stool; the bacteria change from Gram negative to Gram positive. Most of the babies had no fever; in a few the giving of casein-milk was followed by a slight increase in the temperature. There was a gain in weight in some and loss in others. In the latter instance sugar should be added to the food. Birk concludes that casein-milk is valuable in some instances; is indicated in "acuten toxicosen" and in chronic digestive disturbances in which there is an intolerance for cow-milk fat.

Fritz B. Talbot.

Some Questions of Human Milk Secretion, Especially Milk-Fat

(Dr. St. Engel. *Arch. f. Kinderh.*, 1910, liii, Nos. 4-6)

The author investigated the amount of milk given by five wet-nurses at the different nursings during the day, all that was obtainable being taken at each feeding; 504 observations were made. His conclusions are: 1. The largest amount of milk was always given at the first feeding in the morning; less at the last feeding in the evening; during the day the amounts varied but were always less than those given in the morning and the evening. 2. The percentage of fat in the milk varied in inverse proportion to the amount; that is, it was least in the morning feeding, a little greater in the evening, greatest in the feedings during the day.

The second part of the investigation concerned the influence of diet on the percentage of fat in human milk. Contrary to the opinion of other investigators, especially Moll, St. Engel concludes that if the diet of a nursing woman is already sufficient, any addition of fat or other food stuffs has no effect on the percentage of fat.

G. L. Meigs.

Suitability of Condensed Milk for Infant Feeding

(James O. Jordan and Frank E. Mott. *Am. Jour. Pub. Hyg.*, 1910, xx, 391)

An investigation was undertaken to determine whether the substitution of the common varieties of condensed milk for fresh milk and cream was founded on an economic basis and whether the substitute was suitable for infant feeding. Jordan and Mott first analyzed the milks as sold in the cans and from the results reckoned the fat in the original milk from which the condensed milk was made. The fat content was taken as the factor of chief importance because on it the commercial value of milk is calculated. They found that either milk of abnormally low grade was used or milk from which a portion of the cream had first been removed. The cost of condensed milk was then ascertained by determining the price per quart, provided it was diluted with only enough water to make the fat 3.35 per cent (the standard required by the Massachusetts law). The cheapest milk so made exceeds the price of ordinary milk and in some instances is more than the price of certified milk. If the dilutions advocated on the can are made the resulting mixture about equals a mixture of plain milk with one-third to equal parts of water. The greatest interest in this matter arises from the employment of condensed milk for infant feeding. If diluted as directed for this

purpose, the resulting mixture is an imitation of starvation diet. The manufacturers could not have advocated the employment of milk so diluted without being aware of its small food value. The formula from a common brand, the "Red Cross," for a baby 6 months old is, fat 0.84 per cent, sugar 1.41 per cent., cane sugar 4.30 per cent., proteids 0.87 per cent., carbohydrates 0.15 per cent., water 92.43 per cent. There is the further objection to the use of sweetened milks in the added cane sugar. Another fact of importance is that while a few of the brands were found sterile, a majority contained large numbers of organisms in many packages. The authors conclude that the only legitimate field for condensed milk is that of supplying a product where fresh milk is not available. The misleading statements by the manufacturers should be prohibited by law. Packages should bear a formula for diluting with water so that the resulting mixture shall not be below standard for milk solid or fat.

RICHARD M. SMITH.

Hypothyroidism in Nurslings and in Infants After Weaning

(L. M. Spolverini. *Revue d'hyg. et de méd. Inf.*, 1910, ix, No. 3, p. 201)

Spolverini states that the signs of diminished thyroid secretion in infants do not appear until the end of the first year, or until after weaning. This he ascribes to substances furnished the child in breast-milk. He includes the mammary glands among the glands of internal secretion, influenced by the thyroid, and believes that diminished or increased thyroid secretion in the mother or nurse affects the nursling.

He divides infants into three groups: A. Those of a normal thyroid secretion, namely (1) mother or nurse and child with a normal thyroid; (2) mother or nurse with a normal thyroid and child with a hypo- or hyperthyroidism; (3) mother or nurse with a slight hypo- or hyperthyroidism and child with a normal thyroid. B. Those infants with a diminished thyroid secretion having for a determining cause the milk of the mother or nurse affected with insufficient thyroid secretion, and for predisposing cause a congenital hypothyroidism in the child. C. The group of infants with increased thyroid secretion, having for a determining cause the milk of a woman affected with hyperthyroidism, and for predisposing cause an unstable thyroid secretion, usually congenital in the child.

Spolverini deals entirely with children showing insufficient thyroid secretion and has studied in all nine patients, five of whom were still nursed and four already weaned. In addition four normal patients were used as controls. Thyroid extract was given in amounts, depending on the severity of the case and the age of the child, for periods of six days, followed by a day or more of rest. Nursing mothers, as well as the child, were given the drug. All patients showed a marked improvement; all gained weight, but those infants already weaned showed first a loss of weight. Improvement was most marked in the nursling whose mother or nurse received thyroid extract at the same time. All the controls showed a loss of weight during the treatment.

Heredity is the most important etiologic factor, and, of hereditary influences, disturbances of thyroid secretion in the mother hold first place. Other causes are alcoholism, tuberculosis, malaria and syphilis in either parent.

As the most important diagnostic signs in mild cases, in adults as well as children, he gives the following: the hard edema, often transitory; absence of the external third of the eyebrows; falling out or delayed appearance of hair; cold extremities; sensibility to cold; delayed dentition; constipation; anorexia; propensity to fatigue; headache; lack of muscular tone; pain in joints; apathy; drowsiness; absence of gain in weight, or occasionally, on the other hand, obesity; and retardation of mental and physical development.

In all these cases, mothers as well as children, an attempt was made by blood-serum tests to prove the variation of the complement while under treatment. This followed the line of work undertaken by Fassin, who found an increase in

the serum complement of thyroidectomized dogs and rabbits after the injection of thyroid extract.

In these cases Spolverini was unable to demonstrate any increase in the complement after the administration of thyroid extract. He did show, however, that the complement in the blood of the mother and of the nursing was nearly identical, but when the child was taken from the breast, the complement in the blood of the child showed a marked diminution from that of the mother.

J. HERBERT YOUNG.

Schematic Representation of Infant Feeding for Purposes of Instruction

(C. v. Pirquet. *Ztschr. f. Kinderh.*, 1910, *i*, No. 1, p. 111)

Based on the fundamentals as taught by Camerer, Heubner, Czerny and Finkelstein, v. Pirquet shows by a series of figures the essentials of these new ideas.

Figure 1 represents the reactions of the normal child to increasing amounts of food. As indicated there is (1) a minimum, the smallest amount of the food necessary for the infant to gain weight; (2) an optimum, the amount it can handle with the greatest advantage; (3) a maximum, the tolerance limit, which is the greatest amount of the same food that the infant can take care of without drop in weight or bodily harm. The figure shows the loss in weight incident to passing either beyond the maximum or staying below the minimum. As long as the amount of food is kept within the nutritional range there can be no danger to the child *ex elimetitione*. The second figure, practically a continuation of the first, shows the effect of continued overfeeding, causing an acute intoxication with a gradual lowering of the tolerance until it falls far below the minimum. The food that in smaller amounts could have nourished the child acts like a poison when given in these large amounts.

Figure 3 shows the beneficial effect of reducing the food to a minimum, after over-feeding has produced a fat indigestion; explaining how with one-half the amount of the original food an infant can gain weight, when before it was standing still.

Figure 4 illustrates a more severe case of fat indigestion, in which reduction of the amount of milk is not sufficient, but the complete withdrawal of food is necessary to bring the tolerance back above the minimum, so that a large enough amount of food can be taken care of to produce a gain in weight.

Figure 5 represents the result of waiting too long in a case such as is illustrated in figure 4; the tolerance has been allowed to drop so low, that nothing can raise it above the minimum, which means that the child must die of inanition, because before sufficient of the food can be utilized to supply the waste it will act toxically.

Figures 6 and 7 show to a nicety what happens during an infection and during periods of high external temperature. The tolerance drops markedly and unless the food is reduced in the same measure gastro-intestinal disturbance will result.

Figure 8 illustrates the advantages of breast-milk in the therapy of gastro-intestinal disturbances. The tolerance limit is indicated for mother's milk one-half and one-third cow's milk. At point *a* the infant is exposed to high summer temperature, the tolerance for the food that it was taking falls far below the minimum, and only long days of starvation would bring it back within the nutritional range. By giving breast milk, however, a child can immediately be given quantities necessary to produce a gain in weight.

In Figure 9 v. Pirquet illustrates the relative low tolerance for cow's milk of the new-born infant, and its gradual rise with increasing age. The point at which the tolerance limit of a certain food crosses the minimum line, is the age at which the child can be raised with this food.

As v. Pirquet states, this contribution is a mere beginning, but a very excellent one, and one that will do much to make the teaching of the difficult subject of infant feeding a great deal easier than it has been heretofore.

H. F. HELMHOLTZ.



Fig. 1. Minimum, optimum and maximum of food.

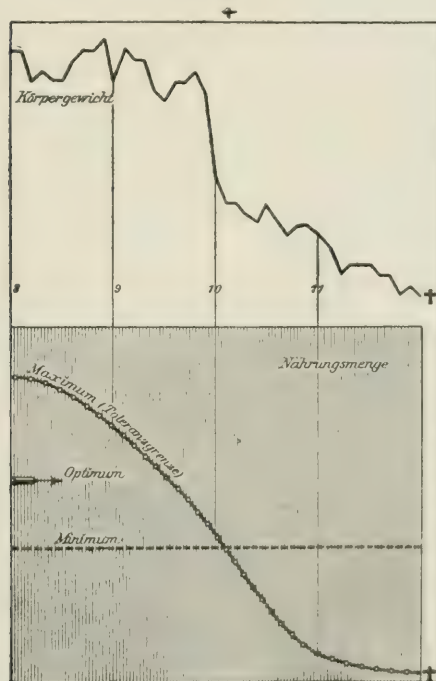


Fig. 2. Fatal gastro-enteritis due to over-feeding.

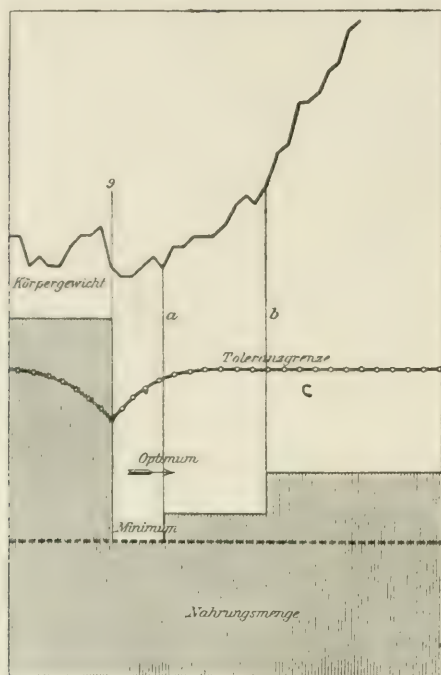


Fig. 3. Therapy in beginning fat-indigestion.

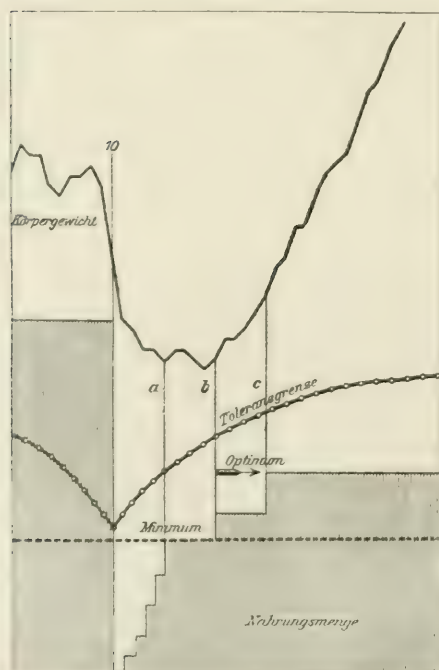


Fig. 4. Therapy in a more advanced case of fat-indigestion.

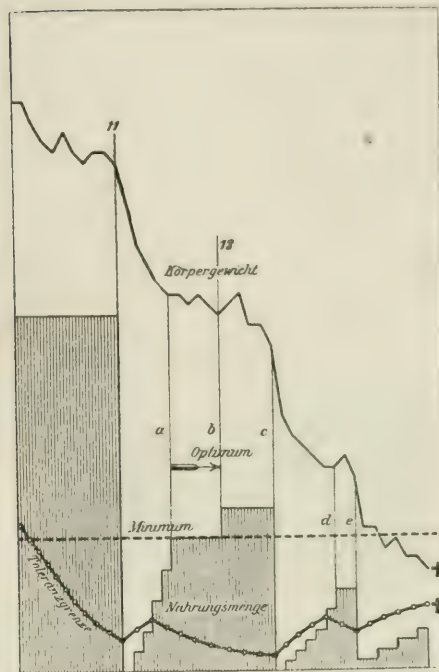


Fig. 5. Ineffectiveness of therapy when instituted too late.

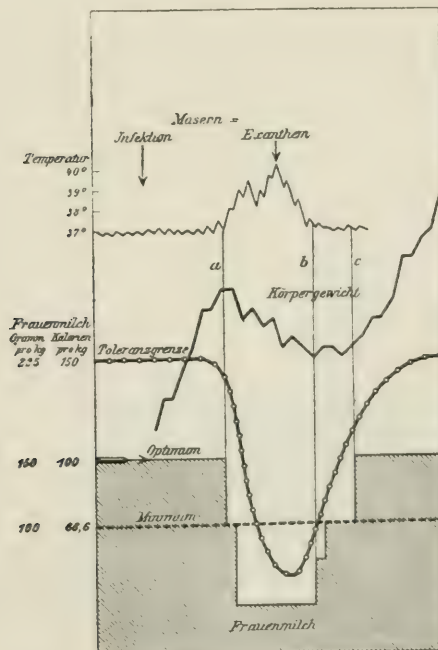


Fig. 6. Lowering of tolerance limit by an acute infection in a breast-fed child.

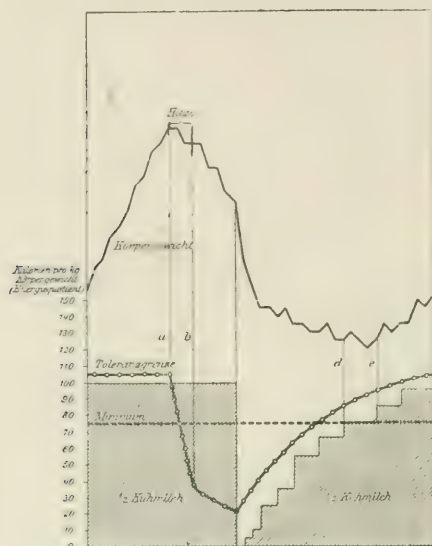


Fig. 7. Lowering of the tolerance limit by external heat in a bottle-fed child.

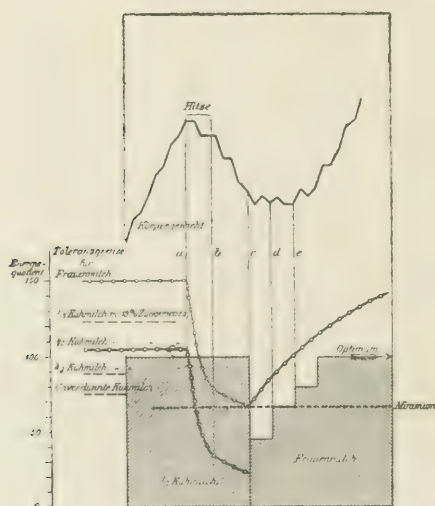


Fig. 8. Tolerance limits of a 6 weeks' old infant. The curing of an intercurrent disturbance by a return to mother's milk.

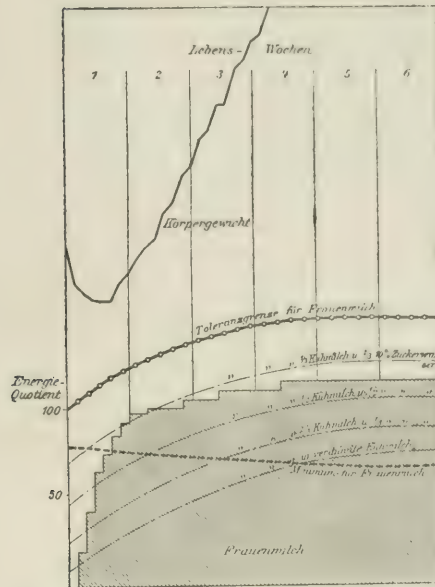


Fig. 9. Tolerance limits of a new-born infant and their gradual rise when breast-milk is fed.

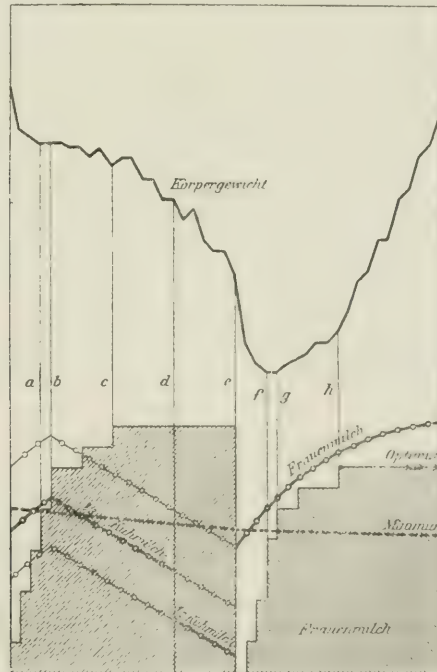


Fig. 10. Showing the effect of over-feeding with cow's milk in the new-born infant and improvement from breast-milk.

ACUTE INFECTIOUS DISEASES

Experience With 678 Tracheotomies During the Years 1899-1908

(J. C. Schippers, Amsterdam, *Jahrb. f. Kinderh.*, 1910, lxxii, No. 5)

A study of these reports tends to show that intubation is not necessarily preferable to tracheotomy. The majority of the cases were diphtheritic laryngeal stenosis; almost invariably "tracheotomy inferior" was done, while a limited few had "tracheotomy superior." Anesthesia was seldom resorted to, and mostly in cases in which very strong children showed great resistance. One to 2 c.c. of chloroform sufficed as a rule, while very often the anesthesia due to the carbon dioxid was enough. All cases were first treated with antidiphtheritic serum, and also when possible with inhalations, ice-bags, warm baths, cold sprays, etc., to prevent the necessity of operation. The length of time necessary to wear the tube was interesting. While in 1899 the average length was five days, in 1908 it was 3.6 days. The time the 400 cases required nursing care averaged practically three weeks. The mortality in 492 cases, without lung complications preceding, was 18 per cent. Prognosis was of course clouded by lung complications, and by the duration of laryngeal stenosis; in the former it was 50 per cent. The mortality of patients operated on was no higher than that shown in intubation, and the latter method certainly has many more disagreeable features.

A. C. SOPER, JR.

New Views Regarding Treatment of Scarlatina

(G. Jochmann and G. Michaelis, *Berl. klin. Wchnschr.*, 1910, xlvii, No. 20)

These authors regard the streptococcus as the chief factor of scarlatina, in spite of the fact that in a majority of the "foudroyant" fatal cases streptococci are not found. Their therapy is directed against the streptococcus by means of vaccines and serums. The serums of Marmorek, Aronson, von Leyden and others, tried in recent years, have been of no particular value. Then the Wright vaccine therapy was tried, controlled by the index technic in 130 cases, only establishing the fact that the index to streptococcus is low in scarlatina, and that it can be raised by opsonic therapy. No definite therapeutic benefit was seen. The serum was injected intravenously in the worst cases, those especially which had a bad prognosis from the first, and subcutaneously in the less severe ones. A combination of vaccine-therapy and serotherapy was tried in the majority of the 130 cases (in sixty-two, to be accurate). While the statistics here given did not prove anything definite, the authors feel warranted in regarding the treatment as a success, judging from considerable experience with it. The day of the injection seemed to make no difference. In a few cases injurious effects of the therapy were seen; eight had urticarial serum-exanthemata. No nephritis was found in thirty-eight patients who recovered. This therapy seemed of little or no avail in the severe cases, and was really of value only in those but slightly affected with streptococcemia.

A. C. SOPER, JR.

TUBERCULOSIS AND SYPHILIS

The Treatment of Tuberculous Children With Large Doses of Tuberculin

(A. Fuchs, *Wien. Jahrb. f. Kinderh.*, 1910, lxxii, No. 5)

This work was begun in 1908 with treatment according to the Schlossman technic, and the dosage was generally with 1 gm. and upward; in each case a small dose if followed by no reaction was succeeded by a slightly larger one. No injections were given until the case was afebrile; then a start was made with 1 c.c. of a 1-1000 solution or less; if in forty-eight hours no febrile reaction ensued another injection was given, of twice the amount, and thus the technic proceeded by steps. If fever followed an injection, the next time the same dose was given—or a smaller one—and not until the case was afebrile was the original

dose returned to. As a rule, about two months was necessary to raise the dosage to 1 gm. Delay of the immunization process was seen in lung complications; an occasional case offered special resistance and an inconceivably small dose caused the worst reaction, so that finally the treatment was stopped. No improvement was seen in any case; in general the condition was made worse. In the method here used, no therapeutic effect was seen in the surgical cases; in some cases, indeed, an exacerbation of the disease was seen, with propagation to other parts of the body. The same was true of pulmonary tuberculosis. Peculiar anaphylactic skin reactions occurred with great regularity in "local" injections.

A. C. SOPER, JR.

Colles' Law and the New Syphilitic Facts

(W. Knopfmacher and H. Lehdorf. *Jahrb. f. Kinderh.*, 1910, lxxi, No. 2)

This work deals with the question whether hereditary syphilis is a placental or a germinal transmission of infection, helping to clear up the theories on the basis of the discovery of the specific microorganism. Matzenauer and others discussed this fully, earlier, and seem to have decided more in favor of a placental than a germinal transmission. Three points are considered: 1. Inflammatory changes in the placenta and umbilical cord are very common even if not pathognomonic. 2. Spirochetes are found in the fetal parts, and especially in the fetal ovaries and testicles, although not yet demonstrated in such parts in the adult. Of especial interest is the finding of the spirochete in the placenta—seldom in the maternal parts, but more generally in the fetal; nevertheless, no sure conclusions are possible as to the exact origin of hereditary syphilis. 3. The Wassermann reaction was positive in 62 per cent. of 116 women whose children had hereditary syphilis. These were divided into two groups, of whom the first had not shown demonstrable syphilis and the second had; group 1 had 59 per cent. positive and group 2 had 72 per cent. They conclude that the mothers of syphilitic children, whether denying syphilis or not, showed practically the same response to the Wassermann. Also, the number of births of syphilitic children per woman was no factor; only women bearing eight or more showing a lower per cent. (46 per cent.). The percentage varies from 90 per cent. positive in women examined a short time after the birth of a syphilitic child, to 40 to 50 per cent. of those examined many years after such births. Probably all such react the same as syphilitic patients. Also, syphilis is believed to be transmitted by and from the mother, and not by paternal germination. The evidence that without exception all children with hereditary lues are infected *ex matre* and by the placental route stands fast and is not to be confuted; and the possibility of a paternal origin must be regarded with greater incredulity than before.

A. C. SOPER, JR.

Hereditary Syphilis and the Wassermann Reaction

(P. Mulzer and W. Michaelis. *Berl. klin. Wchnschr.*, 1910, xlvii, No. 30)

The patients chosen were all syphilitic, or supposed to be; the majority were infants (excluding new-born); forty-four patients with manifest syphilis showed forty-two positive and two negative Wassermann reactions. Also, in fresh congenital syphilis, 95 per cent. were positive. In this last group were three especially interesting cases; one, a child 2 months old, had given a negative Wassermann reaction three weeks before the outbreak of the syphilis, i. e., while it yet showed no syphilitic symptoms. The serologic examination was made because the mother had rigid pupil-reflex and the father was in an insane asylum with cerebral softening. In this case with the onset of syphilitic symptoms came the first positive reaction. The same was true of a second patient whose two older sisters were syphilitic and who nevertheless showed no symptoms; at first negative, the reaction was positive only later, when a coryza had begun. A third patient was examined because it was a 7 months' birth and the father was syphilitic. The serum reaction was positive although no syphilitic symptoms were present. The cases of latent hereditary syphilis were equally

interesting. Positive reaction was found in 59 per cent. Referring to the patients treated, it could not be demonstrated that a negative reaction was produced; of nineteen patients only six showed first a positive and later a negative reaction. Conclusions: of mothers of syphilitic infants 90-100 per cent. react positively; this is also true of women who within four years have borne syphilitic children. Also, symptomless children of syphilitic mothers, showing negative reaction shortly after birth, show a positive reaction a few weeks later, and mostly at the onset of syphilitic symptoms.

A. C. SOPEB, JR.

GASTROINTESTINAL SYSTEM

Bacteriology of Bacillary Dysentery

(A. L. Kendall. *Boston Med. and Surg. Jour.*, 1910, *clxiii*, 398)

Kendall states briefly the principles underlying the activity of the dysentery bacillus as associated with the disease, bacillary dysentery. The foundation for the work rests on these principles: 1. Bacteria in presence of protein and fermentable carbohydrate act on carbohydrate, in the vast majority of cases attacking the protein only sufficiently to satisfy their nitrogen requirements. 2. In the body carbohydrate also can be used to prevent metabolism of nitrogen. 3. Dysentery bacilli attack fermentable carbohydrate in preference to protein. 4. Bacteria attacking protein form toxic putrefactive products, but not if grown in media containing carbohydrate which they can utilize. The products of the dysentery bacillus which are harmful are largely protein decomposition products and can be prevented by utilization of sugar instead. 5. The blood of normal human beings contains about 0.2 per cent. dextrose. 6. The normal sugar for man is lactose, an animal sugar. It is utilizable by few bacteria except those of intestinal origin. The bacterial flora of the intestinal tract in bacillary dysentery is putrefactive, because of the small amount of sugar present. This is also true within the body, for the dextrose is early used up, especially if the patient is on starvation diet. The remedy, bacteriologically speaking, is to add an excess of sugar to the intestinal tract and restore the normal amount of dextrose to the blood. Chemically pure dextrose can be supplied in 2.5 per cent. strength in normal saline solution, given subcutaneously. This furnishes fuel to be used immediately by the body and also food for the invading organisms, thus sparing the body tissue. Feeding lactose by mouth (5 per cent. solution) brings about a similar change in the intestinal bacteria, converting a putrefactive into a fermentative type and producing lactic acid, an antagonist to the dysentery bacillus. Coincidentally with this change the intestinal flora approaches that of normal infants—*B. bifidus* and *B. acidophilus* begin to appear in the stools. These organisms also produce lactic acid, still further antagonizing the dysentery bacillus.

RICHARD M. SMITH.

CIRCULATORY SYSTEM

Blood-Pressure in Childhood

(Fr. Wolfensohn-Kriss. *Arch. f. Kinderh.*, 1910, *liii*, Nos. 4-6.)

The author studied the blood-pressures of 350 children in order to determine the normal blood-pressure, and the influence on it of age, size and weight. The children varied in age from a few weeks to 14 years and the blood-pressure from 80 to 113 mm. of mercury.

The author's conclusions are: 1. The blood-pressure increases in direct proportion to the age, size and weight. 2. Age alone has no influence on the blood-pressure, which depends rather on the size and weight. 3. Sex has no influence on blood-pressure, provided size and weight are the same. The author also studied the blood-pressure of sixty-five sick children, but found that the number was too small to allow of any conclusions. In eight cases of tuberculosis, and in ten cases of bronchitis the blood-pressure was normal for the age.

G. L. MEIGS.

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CONGENITAL PYLORIC STENOSIS *

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CHICAGO

REVIEW OF LITERATURE

Reports of post-mortem findings showing pyloric stenosis with hypertrophy of the musculature, which was believed to be congenital, are found in the literature as early as 1811. Osler and Scudder accept references even much earlier. Landerer collected reports of ten such cases in 1879, and later Maier reported twenty-one cases found by himself in the dead-house. None of these was in an infant. In 1887 Hirschsprung of Copenhagen reported two cases in infants, and practically placed the condition in the category of recognized pathologic lesions. Since that time a considerable literature on the subject has developed.

In 1896 F. Schweyzer¹ first suggested operative treatment for the relief of the obstruction either by divulsion or gastro-enterostomy.

In 1897 Stern² operated on the first patient with unfortunately a fatal result. In 1898 Willy Meyer operated, using a Murphy button, also with a fatal termination. In 1898 Lobker first operated successfully on a child eleven weeks old. In 1901, M. Schmidt³ collected from the literature eight cases of gastro-enterostomy for congenital pyloric stenosis with four recoveries and four deaths and one case of pyloroplasty with death.

Practically, then, the operative treatment of congenital pyloric stenosis is little more than ten years old.

Pfaundler⁴ in 1897, after the report of Stern's unsuccessful case, investigated and reported fully on this subject. His article is a severe criticism of Stern's work. Pfaundler comes to the conclusion that there is no warrant for assuming the existence of an organic congenital pyloric stenosis. He believes that in the cadaver of an infant a permanent contraction of the musculature at the pylorus can persist even after death, which may appear as a hyperplastic tumor obstructing the lumen. He believes that the cases of congenital pyloric stenosis reported by Hirschsprung and Stern and others are to be explained in this way.

* Read in the Section on Diseases of Children of the American Medical Association, at the Sixty-first Annual Session, held at St. Louis, June, 1910.

1. Schweyzer, F.: New York Med. Jour., Nov. 21, 1896.

2. Deutsch. med. Wchnschr., 1898, No. 38, p. 601.

3. Schmidt, M.: Arch. f. klin. Chir., 1901, lxiii, 976.

4. Pfaundler: Wien. klin. Wchnschr., 1898, No. 45, p. 1025.

Pfaundler's erroneous and fantastic conception of this condition has done much harm and has misled many pediatricists into regarding the cases of true hypertrophic stenosis as cases of spasm and has prevented in this way the more general adoption of the early and proper operative treatment. Thomson⁵ in 1897 came to much the same conclusion. He must have changed his views later, however, as he has since had his colleague, Stiles, operate in many of his cases. Heubner and his followers at first regarded the condition as due to pyloric spasm, and Mikulicz in the first edition of the Von Bergmann-Bruns-Mikulicz handbook of surgery stated that he had not encountered the condition and was not prepared to discuss the question as to whether an operation was warranted or not.

Pfaundler in his first paper had gone so far as to state that "in none of these cases was there any warrant for a serious operation." Trautenroth⁶ reports a case in which operation was successfully done and collects reports of twelve cases from the literature with seven recoveries and five deaths. He believes that there is a characteristic symptom-complex in young infants due to a congenital pyloric obstruction, and that a sufficient number of cases have been carefully observed to warrant the conclusion that the obstruction is organic.

In 1903 Walter Freund⁷ of Breslau reports six cases observed in the Breslau clinic and reviews the subject. In 1905 Wachenheim⁸ published a paper on hypertrophy and stenosis of the pylorus in infants, which was read before the pediatric section of the New York Academy of Medicine. He collected reports of about sixty cases from the literature. He reports a fatal case, giving the post-mortem findings, and concludes that in his case an operation would have been the only hope. He believes that cases of congenital pyloric stenosis can be divided into three groups:

1. Those of infants which live for some years, even to adult life, with more or less symptoms of obstruction due to a stenosis of moderate degree.

2. Those of infants which present symptoms of pyloric obstruction which disappear spontaneously.

3. Cases of infants which either die within a few weeks of inanition or are relieved of an almost total obturation by surgical measures.

Wachenheim could collect reports of thirty-two operations with fifteen cures and seventeen deaths. In 1905 Scudder⁹ reports from the literature

5. Thomson: Scot. Med. and Surg. Jour., June, 1897.

6. Trautenroth: Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1902, ix, 724.

7. Freund, W.: Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1903, xi, No. 2.

8. Wachenheim: Am. Jour. Med. Sci., 1905, cxxix, 636.

9. Scudder, C. L., and Quinby, W. C.: Stenosis of the Pylorus in Infancy: An Analysis of 115 Cases, The Journal A. M. A., May 27, 1905, p. 1665, June 3, 1905, p. 1742.

115 cases in which fifty-nine patients were operated on; one patient twice; forty by gastro-enterostomy, with twenty-one deaths; eleven by divulsion, with four deaths; eight by pyloroplasty, with four deaths, and one fatal case of pylorostomy. In 1906 Cautley and Stiles¹⁰ present very full and valuable papers in a symposium on this subject. Cautley has published several times on this subject, in 1898 reporting two cases and collecting reports of seventeen from the literature; and writing again in 1902, when he was able to collect fifty cases; in his paper of 1906 he states that the condition is much more common than generally believed. He himself has had sixteen cases and believes that he could probably collect reports of from 100 to 150 from the literature.

Stiles reviews the subject especially from the surgical standpoint and reports twenty-two cases operated on by himself. In 1908 Bunts of Cleve-

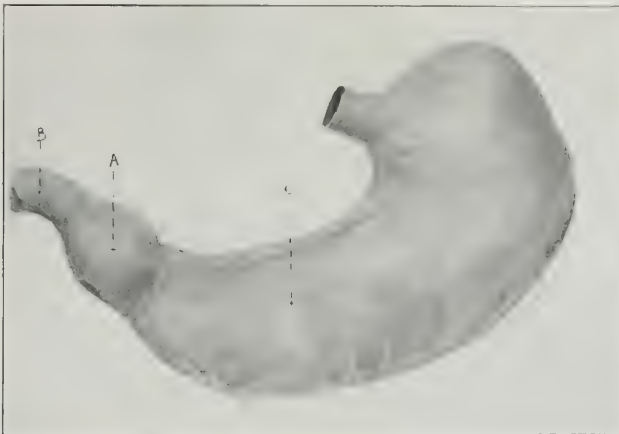


Fig. 1.—Drawing of stomach of a child that died at age of 9 weeks, suffering from congenital stenosis of pylorus. Breast-fed until 3 weeks old, during which time there was persistent vomiting. Weight at birth, 7½ pounds; weight at death, 6½ pounds. Note cranberry-sized swelling. A, at pylorus; B, duodenum; C, stomach. (From Rush Medical College Pathological Museum.) Drawings made by Miss M. von Stoesser.

land read before the American Surgical Association a paper on infantile hypertrophic stenosis of the pylorus. He collected reports of 114 cases, with fifty-three recoveries and sixty-three deaths. In 1908 Cautley presents a further contribution to this subject.¹¹ His paper is on the pathology of congenital hypertrophy of the pylorus in relation to treatment. He says:

Accepting the view that there is such a condition as pyloric spasm in infants, there is no evidence that spasm could cause hypertrophy. Spasm of the pylorus

10. Cautley and Stiles: *Brit. Med. Jour.*, Oct. 13, 1906, p. 939.

11. Cautley: *Brit. Med. Jour.*, Feb. 8, 1908, p. 323.

does occur at all ages, but it does not produce the condition of hypertrophy which is peculiar to the first few weeks of life. Recovery from pyloric spasm under medical treatment in cases mistaken for true hypertrophy has led to an unduly favorable estimate of the value of medical treatment in true hypertrophy. True hypertrophy varies from a degree which is fatal unless relieved surgically to a slight hyperplasia which is compatible with life.

Cautley regards it as of vital importance to differentiate spasm from hypertrophy. He urges that the medical treatment of true hypertrophy

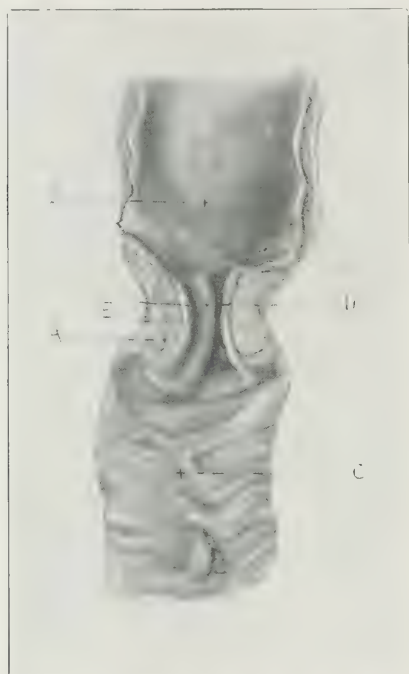


Fig. 2.—Longitudinal section through A, hypertrophied tumor mass at pylorus; B, duodenum and (c) stomach, showing (D) the normal longitudinal folds of mucous membrane hypertrophied in pyloric region of the stomach from stomach shown in Figure 1. E shows area from which tissue was taken for microscopic section as shown in Figure 3.

should not be unduly prolonged. Koplik¹² of New York writes on congenital pyloric spasm and congenital stenosis of the pylorus in infants. He reports a number of cases of pyloric spasm and several of pyloric stenosis, in two of which the patients were operated on by his surgical colleague at the Mount Sinai Hospital, Dr. Lilienthal, with one recovery and one death. In the fatal case the patient died of a middle-ear infection which was operated on and drained.

12. Koplik: Jour. Am. Med. Sc., July, 1908, p. 1.

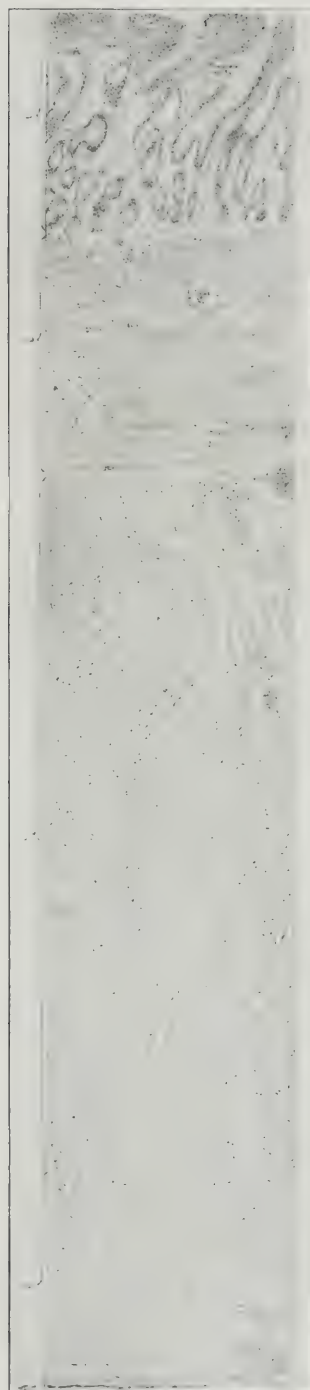


Fig. 3.—Longitudinal (parallel to long axis of howel) section through the hypertrophied pylorus, showing the hypertrophy of circular muscular layer (C). The longitudinal muscular fiber (B) is little if at all changed. A, serosa; B, long muscular layer; C, circular muscular layer; D, hypertrophied submucosa; E, tunica propria.

This brief sketch of the literature I have obtained from reviewing the subject in my own library. It contains, however, the important steps in the development of our present knowledge of the subject. I have operated on four patients with three recoveries and one death.

I shall attempt from my own experience and from a review of the literature to analyze the facts and to present for consideration an estimate of the value of and indications for surgical interference in congenital pyloric stenosis.

INDICATIONS FOR OPERATION

1. *The Existence of a True Hypertrophy.*—In the patients on whom I have operated I have found exactly the same conditions in each case; they were as alike as so many peas. There was a hard cartilaginous tumor at the pylorus about the size and shape of a cranberry (Figs. 1 and 2). Cunningham has shown in his studies of this subject that the pylorus in infancy is well marked, forming a distinct mass of muscle



Fig. 4. Subject from which specimen shown in Figure 1 was taken. This shows clearly the peristaltic waves of stomach.

tissue easily differentiated from the stomach and duodenum; at the same time, as I have had the opportunity of proving to myself, the normal infant pylorus, whether contracted or relaxed, presents nothing like the distinct tumor mass of the case of congenital hypertrophy which produces stenosis. Under the microscope the tumor is due to a greatly hypertrophied muscularis, both layers being involved, but most of the thickening is due to hypertrophy of the circular muscle layer (Fig. 3). Anyone who has seen a typical case, either at operation or post mortem and especially if he has studied a microscopic section, can have no doubts as to the existence of a congenital organic hypertrophy of the pylorus producing stenosis. Pfaundler's views are to-day no longer tenable.

2. *The Symptom-Complex.*—I shall not go into this very fully, as you of the Section on Diseases of Children are much better prepared to draw this picture than I. The symptoms come on from a few days to

six weeks or more after birth. They consist of vomiting after feeding, which at first may be irregular but which gradually becomes regular and persistent. The vomiting is forcible and projectile. The child loses weight, even after change of diet; as the condition progresses visible peristalsis can be seen, sometimes of such an exaggerated character that it can be easily seen and photographed (Fig. 4). The child becomes more and more emaciated (Fig. 5); in a fair proportion of cases a distinct small, hard, firm tumor can be felt at the pylorus. This is not by any means constant and a positive diagnosis must not be withheld because of its absence.

3. *Other Conditions Which Simulate Pyloric Stenosis.*—Undoubtedly other conditions than an organic stenosis at the pylorus can give much the same picture. Spasm of the pylorus from any cause can produce vomiting, peristalsis and loss of weight. The symptoms are seldom as severe and persistent as in cases of organic obstruction. The vomiting is seldom as forcible, the peristalsis is seldom as marked, and the pyloric



Fig. 5.—Child with congenital pyloric stenosis showing high grade of emaciation and dilatation of stomach. (Frank X. Wall's case.)

contraction is seldom as palpable as in organic obstruction. Persistent vomiting in infancy from improper feeding might simulate or rather suggest the possibility of stenosis.

4. *Differentiation from Other Conditions.*—The differentiation in a given case which can be observed for some time must, I think, be determined by excluding other causes of vomiting, such as improper feeding, by careful attention to the child's diet. With the possibility of pyloric spasm in view, unless the condition of the child when first seen demands immediate operative relief, the stomach can be washed out, proper feeding instituted and the case watched for some days in order to establish a positive diagnosis. A sufficiently definite, clinical diagnosis can be made of pyloric obstruction if, after eliminating such possibilities as improper feeding and giving the infant the benefits of gastric lavage and proper diet, the vomiting persists and visible peristalsis of the stomach

van, by pace out with continued loss of weight and progressive weakness. Of course, if a distinct pyloric tumor can be felt, it makes the diagnosis all the more certain.

5. *Treatment*.—After a definite diagnosis has been made, what should be the treatment? In answer to this I should say "operative relief in all cases." It is especially to emphasize this advice that I present this paper. The surgical treatment of stomach lesions has progressed so far that we can say that a patient's chances of cure in any case of obstruction of the pylorus is much greater with surgical than without surgical aid; and this



Fig. 6. Picture of child 5 years old on whom a gastro-enterostomy was performed by the author when the patient was 5 weeks old, on account of a congenital pyloric stenosis. Boy is in excellent health and no untoward symptoms whatsoever.

is equally true whether the obstruction is due to the scar tissue of ulcer or the new growth of a malignant neoplasm or the thickened musculature of a congenital pyloric stenosis.

The unfortunate and discredited views of Pfaundler have even to-day some influence and because of them many infants with the typical picture

of organic pyloric obstruction are allowed to waste away and die while the hopeless effort is being made to cure the condition by diet and internal medication.

To those who have seen both the clinical picture and the operative and post-mortem findings in these cases, there is no longer any question about the existence of a definite organic obstruction as the cause of the clinical picture; and it is also quite as clear that the only hope of relief is some surgical operation which will overcome the obstruction.

6. *Operation.*—What form of surgical treatment should be adopted? This can be answered to-day with a good deal of positiveness. In the early work on these cases a number of divulsions of the pylorus were done—the so-called Loreta operation. It was soon found, however, that this was not a reliable procedure; that many of the patients who were apparently cured, relapsed, so that the divulsion operation has been quite generally discarded. There remain practically but two methods to consider, pyloroplasty and gastro-enterostomy. Pyloroplasty has a number of advocates. It leaves the stomach and intestinal canal more nearly normal than does gastro-enterostomy, which leaves a loop of bowel between the pylorus and the new opening, which is to a certain extent side-tracked from the rest of the alimentary canal. Pyloroplasty is, however, difficult to do in the presence of such a great thickening of the muscularis at the pylorus; and, inasmuch as the objection just mentioned to gastro-enterostomy is more theoretical than real, and inasmuch as gastro-enterostomy can be done so rapidly and safely by modern surgical technic, it has gradually become the favorite operation for the relief of most forms of pyloric stenosis. Pyloroplasty, and especially the Finney modified pyloroplasty, are well-recognized surgical procedures in this condition, and have a number of advocates. There can be no doubt, however, that there is greater danger of recurrence of symptoms due to a recurrence of the obstruction after pyloroplasty than after gastro-enterostomy.

7. *Technic of Gastro-Enterostomy.*—This presents no special difficulties in these cases to one who has had some experience with them. The infant's intestines and stomach are of course very small, and special instruments are desirable. Very small forceps and very small intestinal and stomach clamps, which will exert no dangerous pressure on the viscera, should be employed. The posterior no-loop operation with clamps should be made with the needle and thread; no mechanical device like the Murphy button can be employed because of the small caliber of the infant intestine. Ether is the anesthetic of choice in these cases, and when possible the stomach should be washed out just before the operation and sufficient fluids introduced into the child's system by rectal injections and, if necessary, physiologic salt solution subcutaneously. A skilled operator can do a gastro-enterostomy in from twenty to twenty-five minutes.

Special care should be taken to secure a good closure of the abdominal incision, which should be of course in the mid-line above the umbilicus and of sufficient length to permit of rapid operating. I mention this point because many of these children are in such poor general condition that wound healing is apt to be slow and insecure and postoperative hernia may occur.

8. *After-Treatment*.—This is important. The child should be given normal salt solution per rectum, and if this is not well retained, to supply subcutaneously the fluid which is so much needed by these little patients. Within six or eight hours after the operation water and milk can and should be given by mouth. Usually this will be well borne and the child will begin to improve from the first day. There is no danger from leakage at the gastro-intestinal opening from early feeding, as the modern technic insures a perfectly water-tight joint and wound healing goes on much more rapidly if the child is fed early.

9. *Prognosis*.—This depends almost entirely on the condition of the patient. There is little mortality from the operation; the mortality is almost entirely due to the disease. I have no doubt that a skilled surgeon could make a hundred consecutive gastro-enterostomies on children in good general condition with much less than 10 per cent. of mortality; and if all these cases of congenital pyloric stenosis were early recognized and the patients operated on early the mortality would not be much greater; as it is, so many of the patients are in such extremely bad condition when they come to the surgeon, that the mortality is in the neighborhood of 50 per cent. The moral is, of course, early recognition and early operation in cases of congenital pyloric stenosis.

10. *Final Results*.—The end results are excellent. Such an enormous amount of work has now been done in cases of benign pyloric obstruction and its relief by posterior gastro-enterostomy, that we can say that these individuals have a perfectly functioning stomach, that they suffer in no way because the opening is 6 or 12 inches away from the normal opening. The children I have operated on have developed in every way as normal healthy children.

In brief, my conclusions are that congenital pyloric obstruction is a definite, well-established pathologic condition; that it produces, for him who has seen it, an easily recognized clinical picture; that it can as a rule be definitely differentiated from other conditions simulating it; that if early recognized it can be permanently relieved by overcoming the obstruction by modern surgical methods; and that the individual so saved can grow up and develop in a perfectly normal way (Fig. 6).

I pray you give to these poor little chaps, who are born with this defective plumbing, the benefit of a good job of plumbing done early under the best aseptic and operative technic.

150 Michigan Avenue.

CEREBROSPINAL MENINGITIS, ITS ETIOLOGY, DIAGNOSIS, PROGNOSIS AND TREATMENT

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THE CLASSIFICATION OF THE FORMS OF CEREBROSPINAL MENINGITIS

Cerebrospinal meningitis is an infectious disease of the pia mater and arachnoid membranes of the brain and spinal cord. The confused basis of the classification of diseases, which is a legacy from former times, has led to considerable obscurity in the nomenclature used in describing these infections. In the past diseases have been successively classified on bases which have been changed from time to time as our knowledge has increased. We have had classifications based on symptomatology, on vague, unsupported and false notions as to etiology, on morbid anatomic lesion, and on etiology. These former classifications are still to be traced in descriptive terminology, from the fact that we are prone to cling to the names after the ideas which they represent have been superseded by more exact knowledge. Thus the term cerebrospinal meningitis dates from that era in which diseases were classified mainly on the basis of their anatomic lesions, and might falsely convey the idea that it represents a single disease entity. It was early recognized that the lesions found in the meninges differed under certain conditions. In some forms the lesion was a purulent inflammation, in others the exudate was serous, and in still others the condition was represented by specific tissue changes, such as the formation of tubercles. An attempt to adjust the classification to these facts gave rise to the subdivisions of cerebrospinal meningitis described by such terms as simple meningitis, serous meningitis, purulent meningitis and tuberculous meningitis. Later, with the progress in our knowledge of etiology through the increasing revelations made by the study of bacteriology, and the close union between the pathologist and the bacteriologist, came the recognition that ultimate etiology was a more important factor in determining what constitutes a disease entity, and a demand for an etiologic basis of classification arose.

There have been certain difficulties in the way of a complete adoption of such a basis for classifying diseases, which are well illustrated in the case of cerebrospinal meningitis. In the infectious diseases these difficulties are less noticeable than in other diseases in which a multiplicity of etiologic factors lead to disturbance of function, but they are none the less present. If each pathogenic organism invariably led to specific tissue

changes, with characteristic symptoms, there would be no trouble in an etiologic classification, but this is not the case. Some organisms produce characteristic tissue changes, and others do not, and this has led to a hesitation on the part of writers of text-books frankly to adopt an etiologic classification of infectious diseases. Such a classification would demand the description of each condition under the heading of its cause. In instances, however, in which several causes give rise to identical lesions, and the symptoms depend rather on the lesions than on the specific nature of the infection, such a method of classification would necessitate repetition of the description of lesions and symptoms for each organism, which repetition has not been deemed advisable in text-book description. The same description is still largely made to do for various infections of different etiologies, and this tends to perpetuate the idea that the disease entity is determined by these classical descriptions, rather than by the causative pathogenic organism.

This hesitation to adopt an etiologic basis of classification is clearly shown in the text-book descriptions of cerebrospinal meningitis, although recognition of the importance of etiology is shown in a sort of half-hearted attempt to separate off some etiologic forms as specific disease entities. I have found that the most frequent classification is that under the three headings of tuberculous meningitis, epidemic cerebrospinal meningitis, and purulent meningitis. The writers employing this classification recognize the specific nature of the lesion in tubercular infections of the meninges, but hesitate, in the majority of text-books, to place the tuberculous meningitis under the general heading of tuberculosis, preferring to keep it under diseases of the nervous system, for convenience of description. The separation of the epidemic cerebrospinal meningitis from the other forms is unwarranted on the ground of specific lesions, and, as will appear below, is also unwarranted on the ground of any characteristic symptomatology. The only peculiarities warranting such discrimination are the tendency of this infection at times to occur in epidemics and the recent advance made in its treatment by therapeutic measures directed against the specific etiologic agent. The term purulent meningitis is a very bad one, as the epidemic form is also purulent. An improvement in this classification could easily be made by substituting the term "meningitis due to other organisms" for the term purulent meningitis.

It may be that such a classification as this is the only one fitted for text-book description. I am firmly convinced, however, that the time has come to adopt a frankly etiologic classification of the infectious diseases, and that each etiologic form of cerebrospinal meningitis should be described as a separate disease entity. Some way of avoiding the repetition of descriptions of lesions and symptoms can easily be devised for text-

book use, by referring to a previous chapter for these parts of the account of the disease. The advantages of such a clear, uniform and scientific method of classification, should more than offset the difficulties of clear text-book description. A further argument in favor of such a classification, is that all recent therapeutic endeavor is directed against causes rather than lesions or symptoms, and that the greatest therapeutic achievements of recent times have been the discovery of a specific treatment directed against a specific etiologic disease entity. It is fast becoming necessary to describe treatment under the heading of the specific infectious agent, and modern treatment will continue to demand that the descriptions of the disease be also placed under such headings.

THE ETIOLOGIC FORMS OF CEREBROSPINAL MENINGITIS

Cerebrospinal meningitis has a variety of etiologic forms. A number of pathogenic organisms can infect the meninges of the brain and spinal cord. I am unable to give an authentic complete list of the organisms which have caused cerebrospinal meningitis, but will confine myself to the commoner forms of infection. The others are so exceedingly rare as to be isolated curiosities in pathology, rather than disease entities with which the practitioner must expect to cope. The commoner causes of cerebrospinal meningitis are the *Bacillus tuberculosis*, the *Diplococcus intracellularis*, the *Pneumococcus*, the *Streptococcus pyogenes*, the *Bacillus influenzae* (Pfeiffer) and the *Staphylococcus pyogenes*.

The basis of this paper is a series of 142 consecutive cases of cerebrospinal meningitis, which I have seen outside my regular hospital services, in connection with my work as the distributing agent for the Flexner antimeningitis serum. They were all cases in which a diagnosis of cerebrospinal meningitis of some form had been made by the attending physician, to which I was called for the purpose of administering the serum. Every form of meningitis in the list of the commoner forms given above was included in the series, except the form caused by the *Staphylococcus pyogenes*. This form has, however, been reported with sufficient frequency to warrant its having a place among the forms common enough to merit description. In every case in the series a careful and thorough bacteriologic examination of the cerebrospinal fluid was made, and in all cases, except forty-five of the tubercular form, the infecting organism was found in pure culture in the fluid.

FREQUENCY OF THE OCCURRENCE OF THE DIFFERENT FORMS OF CEREBRO-SPINAL MENINGITIS

This comparatively small series of cases throws no very valuable light on the frequency of occurrence of the various forms, because it represents the experience of only a single observer, in a comparatively limited

locality. The relative frequency probably varies greatly at different times, and in different localities. Of course by no means all, or even the greater part, of the cases occurring in this vicinity were reported to me. On the other hand, the physicians in this vicinity were in general thoroughly aroused to the fact that the Flexner serum was achieving very favorable results in the cure of epidemic meningitis, and were on the watch for such cases, recognizing the importance of an early diagnosis, while they were as yet not sufficiently acquainted with the technic of the administration of the serum to undertake it themselves. Also, no epidemic of the form caused by the *Diplococcus intracellularis* was prevalent at the time. It is difficult to form on any other basis any idea of the probable frequency of occurrence of the various forms, as the cases reported to local health boards are not usually based on proper diagnosis, and it is comparatively rare that so large a series of consecutive cases as mine, all with proper bacteriologic examinations, can be reported. The series throws some, though no final, light on the frequency of occurrence of the various forms in this locality at least, as shown by Table 1.

TABLE 1.—THE FREQUENCY OF OCCURRENCE OF THE VARIOUS FORMS OF CEREBROSPINAL MENINGITIS

Form	Number of Cases
Tuberculous meningitis	60
Epidemic cerebrospinal meningitis.....	60
Pneumococcus meningitis	12
Streptococcus meningitis	6
Influenza meningitis	4
Staphylococcus meningitis	0

AGE

Cerebrospinal meningitis is not universally recognized as being particularly a disease of early life. Table 2 shows the frequency with which children are attacked in comparison with adults, a frequency in childhood quite comparable with that of the admitted diseases of childhood, such as the exanthemata. In general, cerebrospinal meningitis may be regarded as a disease of infancy and childhood, coming particularly into the field of those practicing pediatrics.

TABLE 2.—THE AGES OF OCCURRENCE OF THE VARIOUS FORMS OF CEREBROSPINAL MENINGITIS

Year	Tuberculous	Epidemic	Pneumococcus	Streptococcus	Influenza
Under 2	26	10	1	3	0
2 to 15	27	37	1	3	4
16 to 40.....	7	9	4	0	0
Over 40	0	4	6	0	0

Nearly 80 per cent. of all the cases occurred in children. This greater frequency in early life appeared in all forms except that caused by the pneumococcus, which showed the greater frequency in later life. It is

also interesting to observe the great frequency of tubercular meningitis in the first two years of life. The streptococcus cases also, though few in number, showed an equal frequency in infancy and in childhood. The epidemic form, while occurring at all ages, appeared to be particularly a disease of middle childhood.

SYMPTOMATOLOGY

An important question presented by a series of cases, classified on an etiologic basis, was whether there is any correspondence between the etiologic form of cerebrospinal meningitis and the symptoms, whether any form presents characteristic symptoms peculiar to that form, which would be an aid to its clinical recognition. For the purpose of determining this point, Table 3 has been prepared, showing the comparative frequency of occurrence of the characteristic symptoms and signs of meningitis in the various forms.

TABLE 3.—CHARACTERISTIC SYMPTOMS AND SIGNS OF MENINGITIS IN THE VARIOUS FORMS

Symptoms	Tuberculous	Epidemic	Pneumococcus	Streptococcus	Influenza
Onset—					
Sudden	9	47	11	9	2
Medium	13	10	1	4	1
Gradual	37	3	0	2	1
Temperature—					
High	11	41	12	6	1
Moderate	18	17	0	0	3
Low	19	2	0	0	0
Cloudy mentality or delirium—					
Early	2	50	8	0	0
Developed	52	9	4	6	3
Late	4	0	0	0	1
Absent	0	1	0	0	0
Unconsciousness—					
Early	2	27	8	0	0
Medium	15	0	4	4	3
Late	41	0	0	2	1
Absent	0	24	0	0	0
Headache—					
Present	17	32	8	6	4
Doubtful	18	10	4	0	0
Absent	25	18	0	0	0
Rigid neck—					
Early	7	51	10	1	1
Developed	29	8	2	5	3
Absent	23	1	0	0	0
Kernig's sign—					
Early	7	35	11	0	1
Developed	21	5	1	6	2
Absent	31	0	0	0	1

TABLE 3.—CONTINUED

Symptoms.	Tuberculous	Epidemic	Pneumococcus	Streptococcus	Influenza
Knee-jerks—					
Exaggerated 15	13	5	3	1	
Normal 20	8	0	0	1	
Absent 24	39	7	3	2	
Localizing neurologic signs—					
Early 2	4	0	0	0	
Developed 19	6	1	4	2	
Absent 39	50	11	2	2	
Babinski's sign—					
Present 19	19	3	0	0	
Absent 35	41	9	6	4	
Convulsions—					
Early 8	8	2	0	0	
Developed 12	1	0	5	1	
Absent 40	51	10	1	3	
Vomiting—					
Present 41	38	3	6	4	
Absent 19	22	9	0	0	
Pulse—					
Slow 15	9	0	3	0	
Rapid 43	51	12	3	4	
Cheyne-Stokes breathing—					
Present 18	8	1	2	0	
Absent 42	52	11	4	4	
Petechial eruption—					
Present 0	11	2	0	0	
Absent 60	49	10	6	4	

Of course the cases of pneumococcus, streptococcus, and influenza meningitis are too few in number to give any definite information in such a comparison. There are certain general differences in the symptom complex of the various forms which appear in the table; but there are no positive diagnostic symptoms or signs characteristic of any particular form of cerebrospinal meningitis. Not one single symptom, sign or characteristic is found in any one form, which is not also found in one or more of the other forms. We can only conclude from the tabular view of the symptoms of this series of cases, that there are no clinical symptoms or signs sufficiently characteristic of the several forms of cerebrospinal meningitis to be of diagnostic significance, and the differential diagnosis of these several forms cannot be made on the basis of symptomatology.

There are, however, certain differences in the frequency of certain symptoms and characteristics of the various forms of meningitis which are of interest to the clinician.

The onset was most frequently sudden in the epidemic and pneumococcus forms, more gradual in the tuberculous and streptococcus forms, and equally divided in frequency in the influenza form. The temperature was more often moderate in the tuberculous and influenza forms,

and while more often high in the other forms, was extremely high in all six cases of the streptococcus form. Unconsciousness developed with absolute certainty in all forms except the epidemic, but unconsciousness or clouding of the mentality were more frequent early in the epidemic and pneumococcus forms, and developed later in the tuberculous, streptococcus and influenzal forms. Headache was most frequently absent in the tuberculous form. The rigid neck and Kernig's sign were almost constant symptoms of all forms except the tuberculous, in which they were frequently absent. Convulsions were seen in greater proportion in the streptococcus form. A slow pulse was more frequent in the tuberculous and streptococcus forms.

There were certain other differences not shown in the table, which are of interest, though also not characteristic. There was considerable variation in the rapidity with which the disease ran its course. The most rapid course was seen in the pneumococcus cases, in all of which the course was very brief, death usually occurring within twenty-four hours after the development of unconsciousness. While some of the epidemic cases were of the well-known fulminating type, and unconsciousness developed very early, there is more apt to be a pause or stationary phase in this form, before death supervenes; even its most rapid cases were in general less rapid than the pneumococcus cases. In the tuberculous cases, the course was much slower and often prolonged, whereas the streptococcus and influenza cases, while in general more rapid than the tuberculous, were much slower than the epidemic and pneumococcus cases.

From these differences a certain type may be described for each of the several forms, which represents only the most frequent course of each type. The description of such types can at best only enable the physician to make a vague guess at the etiologic form present, because everything mentioned as characteristic of a typical case of any form of cerebrospinal meningitis may be absent in that form, and present in one of the others. A brief summary of the typical characteristics of each form would be as follows:

1. *Tuberculous Meningitis*, characterized by slow onset, often with vomiting as an early symptom; moderate temperature, until the final stage; gradually developing clouding of the mentality, finally developing into unconsciousness; headache more frequently absent than noted; rigidity of the neck and Kernig's sign either late in development or absent; pulse sometimes slow in the early stages; Cheyne-Stokes breathing frequently absent; petechial eruption always absent; a slow course with gradual development of all signs and symptoms.

2. *Epidemic Meningitis*, characterized by a sudden onset, often with vomiting, headache, and sometimes with convulsions; high temperature,

particularly at the onset; unconsciousness sometimes absent, but developing early when present; early clouding of the mentality; rigidity of the neck and Kernig's sign almost invariably present, and appearing early; convulsions early if present, but usually absent; pulse usually rapid; Cheyne-Stokes breathing rare; petechial eruption seen at times, but most frequently absent; great variations in the violence of the onset, in the severity of the case, and in the length of the course of the disease, with a tendency for all symptoms to reach their maximum severity in the first twenty-four hours, with a pause, followed by death, or improvement.¹

3. *Pneumococcus Cases*, characterized by a sudden onset, often with headache, less often with vomiting, the symptoms not reaching their maximum severity so quickly as in the epidemic form; high temperature; unconsciousness developing early, but less often at the first onset; rigidity of the neck and Kernig's sign almost invariably present, and developing early; convulsions early if present, usually absent; pulse usually rapid; Cheyne-Stokes breathing rare; petechial eruption may be present, usually absent; great rapidity of the course of the disease, death coming soon after the development of unconsciousness.

4. *Streptococcus Meningitis*, characterized by a rapid or gradual onset, less sudden than the epidemic or pneumococcus forms, with vomiting and headache; very high temperature, often extreme; unconsciousness, not at the start, but developing or coming late; rigidity of the neck, and Kernig's sign, not at the start, but developing; convulsions frequent, developing; pulse, rapid or slow; petechial eruption absent; a course of disease notably slower than the pneumococcus cases, and than epidemic cases of the same severity, with steady progress toward the fatal ending.

5. *Influenza Meningitis*, characterized by a rapid, medium, or gradual onset, usually with headache and vomiting; moderate or high temperature; unconsciousness, not at the start, but developing or coming late; rigidity of the neck and Kernig's sign, usually present, developing; convulsions, usually absent; pulse rapid; petechial rash absent; a variable course, in general slower than the epidemic and pneumococcus forms.

THE DIAGNOSIS OF CEREBROSPINAL MENINGITIS

Even if we admit that the several forms of cerebrospinal meningitis cannot be differentiated one from another on a basis of their clinical symptoms and signs, the question arises whether these clinical evidences are sufficient to establish a diagnosis of cerebrospinal meningitis without distinction as to etiologic form. In other words, is it possible on this basis to distinguish cerebrospinal meningitis in some form from other infectious diseases? It is quite well known that several other conditions

1. It must be remembered that this description applies only to serum-treated patients.

at times show some of the symptoms considered more or less characteristic of meningitis.

My experience as the distributor of the Flexner serum throws an interesting light on the frequency with which other diseased conditions were mistaken for cerebrospinal meningitis. During the period in which occurred the 142 cases of cerebrospinal meningitis, I was also called to administer serum in eighty-eight cases which had been diagnosed as cerebrospinal meningitis, but which proved to be other diseased conditions, and not any form of meningitis. The diseases which thus sufficiently simulated meningitis as to lead to a demand for serum, are shown in Table 4.

TABLE 4.—LIST OF DISEASES DIAGNOSED AS CEREBROSPINAL MENINGITIS ON THE BASIS OF THEIR SYMPTOM

Disease	Cases
Lobar pneumonia	29
Gastro-enteric intoxication	15
Anterior poliomyelitis	10
Otitis media	9
Encephalitis	8
Typhoid fever	5
Rheumatic fever	3
Cerebral hemorrhage	3
Solitary tubercle	2
Cerebellar tumor	2
Measles with pneumonia.....	1
Tetanus	1

Table 5 shows the frequency with which the various symptoms and signs of cerebrospinal meningitis occurred in this list of diseases.

TABLE 5.—FREQUENCY OF OCCURRENCE OF SYMPTOMS AND SIGNS OF MENINGITIS IN LIST OF DISEASES MISTAKEN FOR MENINGITIS

	Rigid neck	Clouded Mentality	Unconsciousness	Kernig's Sign	Convulsions	Localizing Neurologic Signs	Headache	Vomiting
Lobar pneumonia	26	29	2	22	8	1	15	23
Gastro-enteric intoxication	10	14	6	8	7	2	1	15
Anterior poliomyelitis	9	1	0	6	1	10	9	8
Otitis media	8	6	0	4	3	0	2	8
Encephalitis	6	8	1	7	6	8	6	8
Typhoid fever	5	5	0	3	1	0	5	4
Rheumatic fever	3	0	0	3	0	0	2	1
Cerebral hemorrhage	0	3	3	1	1	2	0	1
Solitary tubercle	0	2	2	0	2	1	2	2
Cerebellar tumor	0	2	0	0	2	0	2	2
Measles with pneumonia.....	1	1	0	1	1	0	1	1
Tetanus	1	0	0	1	1	0	0	0

It appears from Table 5 that any one of the clinical symptoms or signs considered characteristic of cerebrospinal meningitis, may appear in other diseased conditions than meningitis.

In not all the cases shown in Table 4 was it impossible to make a diagnosis on clinical grounds. In thirty-seven of these cases, by the time I had reached the bedside of the patient, the case had sufficiently developed to allow a positive recognition of the actual disease present, and cerebrospinal meningitis was excluded, and no lumbar puncture was performed. There remained, however, fifty-one cases in which cerebrospinal meningitis could not be excluded, and in which it was deemed advisable not to deprive the patient of the benefit of the Flexner serum unless epidemic meningitis could be first excluded. In these cases, shown in Table 6, lumbar puncture was performed, and the true diagnosis appeared later in the course of the disease.

TABLE 6.—DISEASES SEEN DURING A SERIES OF 142 CASES OF CEREBROSPINAL MENINGITIS, IN WHICH MENINGITIS COULD BE EXCLUDED ONLY BY LUMBAR PUNCTURE

Diseases	Cases
Lobar pneumonia	13
Gastro-enteric intoxication	12
Otitis media	8
Encephalitis	8
Typhoid fever	3
Cerebral hemorrhage	3
Anterior poliomyelitis	1
Solitary tubercle	1
Cerebellar tumor	1
Measles with pneumonia.....	1

It appears from the above considerations, that *without lumbar puncture, a diagnosis of cerebrospinal meningitis is absolutely without value for scientific, statistical, or therapeutic purposes.*

It is not the purpose of the present paper to take up the finer scientific distinctions in the characteristics of the cerebrospinal fluid found in the various forms of meningitis, but only those characteristics requisite for ordinary differential diagnosis.

Table 7 shows the characteristics of the cerebrospinal fluid in the various forms of cerebrospinal meningitis on which rests the diagnosis of meningitis, and the differential diagnosis of the various forms.

The examination of the cerebrospinal fluid for diagnostic purposes is not difficult. At the time of performing the lumbar puncture observation of the clearness or cloudiness of the fluid is made, and a few drops of the fluid should be allowed to fall directly from the needle into a culture tube. I am accustomed to collect all the fluid in a test-tube which has been boiled with the lumbar puncture needle, and which is closed for transportation with a sterilized cork. It is best to perform the cell count, or count of the number of cells per cubic millimeter, as soon as possible after the lumbar puncture, because if the count is made after a fibrinous clot has formed in the fluid, it will not be accurate. The technic of this count in which the ordinary Thoma-Zeiss counting appa-

ratus is used, has been described elsewhere.² After the count, before performing the microscopic examination for cells and microorganisms, it is well to wait until a fibrinous clot has formed, or has failed to form in the fluid. Such a clot, in its process of formation, entangles the cells and bacteria in its meshes, and renders it easier to obtain a large number of these elements in cover-glass preparations. If such a fibrinous clot fails to be found, the fluid should be centrifugalized. A small portion of the fibrinous clot, or of the centrifugalized sediment, should be removed with the platinum wire and rubbed up on the cover-glass.

TABLE 7.—DIAGNOSTIC CHARACTERISTICS OF THE CEREBROSPINAL FLUID IN THE ACTIVE STAGES OF THE VARIOUS FORMS OF CEREBROSPINAL MENINGITIS

	Appearance	Cell Count	Predominant Cell	Micro-organisms
Normal fluid	Clear	Normal	Mononuclear lymphocyte	None found
Tubercular meningitis . .	Clear or slightly cloudy	Increased	Mononuclear lymphocyte	Tubercle bacillus in some (Acid-fast)
Epidemic meningitis	Cloudy	Increased	Polymorpho-nuclear neutrophil	Diplococcus intracellularis (Gram-negative)
Pneumococcus meningitis .	Cloudy	Increased	Polymorpho-nuclear neutrophil	Pneumococcus (Gram-positive)
Streptococcus meningitis .	Cloudy	Increased	Polymorpho-nuclear neutrophil	Streptococcus (Gram-positive)
Influenza meningitis	Cloudy	Increased	Polymorpho-nuclear neutrophil	Influenza bacillus (Gram-negative)
Staphylococcus meningitis .	Cloudy	Increased	Polymorpho-nuclear neutrophil	Staphylococcus (Gram-positive)

The cover-glass is first stained with Loeffler's alkaline methylene blue. This gives information as to the presence or absence of microorganisms, and as to the morphology of any bacteria which may be present. The differential count of polynuclear and mononuclear cells may also be satisfactorily made from this preparation, although if desired, another cover-glass may be stained with Wright's blood stain. If bacteria are found, a second cover-glass should be stained by Gram's method, counter-stained with pyronin, or Bismarck brown, in order to determine the reaction of the organism to this method of staining. Finally, a cover-glass should be stained for the tubercle bacillus. If tuberculous meningitis is suspected, and the bacilli are not found at the first examination, the method of digesting the clot with dilute hydrochloric acid with sub-

2. Dunn, C. H.: The Cytodiagnosis of Tuberculous Meningitis, Arch. Pediat., 1910, xxvii, No. 8.

sequent centrifugalization should be used, and repeated search made in a number of preparations. A portion of the fluid should also be injected into a guinea-pig.

For the finding of the bacteria causing meningitis, I am accustomed to rely more on fresh cover-glass preparations than on the results of the culture. While the pneumococcus and streptococcus grow with certainty in cultures, they are also easily found in cover-glass preparations. The influenza bacillus requires a special culture medium. The *Diplococcus intracellularis* does not grow with certainty on the ordinary culture media. In my series of cases there was no case in which the organisms were found in the cultures without having been found in the cover-glass preparations, but there were a number of cases of epidemic meningitis in which the cultures showed no growth. The cultures should, however, always be made as a control.

Considerable stress has been laid by some writers on the chemical examination of the cerebrospinal fluid. As far as the test for sugar is concerned, I believe that it gives no information of diagnostic significance, and is practically of no importance. The test for albumin, however, is of great importance, an increase in the quantity of albumin being an almost invariable accompaniment of inflammatory processes in the meninges.

Whether or not a fibrinous clot is found in the fluid, should always be observed. When present, such a clot is diagnostic, although it is not always present in cases of meningitis.

It will appear from a study of Table 7 that the features of the cerebrospinal fluid which serve to distinguish cerebrospinal meningitis from normal conditions, and from other diseased conditions than meningitis, are, (1) cloudiness of the fluid; (2) an increase in the cell count; and (3) the demonstrated presence of the microorganism causing the infection. It will further appear that the features which serve to differentiate the various forms of cerebrospinal meningitis from one another are (1) the character of the predominant cell, and (2) the character of the infecting bacteria. Unfortunately, not all of these features of the cerebrospinal fluid are of positive diagnostic value. Cloudiness of the fluid is more frequently absent than present in the tuberculous form of cerebrospinal meningitis. Slight cloudiness of the fluid is, moreover, sometimes present in other diseased conditions than cerebrospinal meningitis. The increase in the number of cells counted per cubic millimeter, while always present in cerebrospinal meningitis, is not positively diagnostic, as an increase in the cell count is at times observed in other diseased conditions. In many of the conditions which clinically suggest the possibility of meningitis, the meningeal symptoms are caused by toxic irritation of the meninges. An increase in the number of cells in the cerebrospinal fluid

is not necessarily an evidence of an infection of the meninges but is an evidence of meningeal irritation. The reaction of the meninges to irritation, of whatever origin, is similar to that of the serous membranes, and is manifested through an increase in the number of cells.

TABLE 8.—CERTAIN CHARACTERISTICS OF THE CEREBROSPINAL FLUID IN CASES SIMULATING MENINGITIS

	Fluid		Cell Count	
	Clear	Cloudy	Normal	Increased
Lobar pneumonia	13	0	13	0
Gastroenteric intoxication	11	1	8	4
Otitis media	8	0	8	0
Encephalitis	8	0	0	8
Typhoid fever	3	0	3	0
Anterior poliomyelitis	9	0	6	3
Solitary tubercle	1	0	1	0
Cerebellar tumor	1	0	1	0
Measles with pneumonia	1	0	1	0
Tetanus	1	0	0	1

In Table 8 is shown the observations of the cerebrospinal fluid as to cloudiness and increased cell count in the fifty-one cases of diseased conditions in which cerebrospinal meningitis could only be excluded by lumbar puncture. It shows the failure of an increased cell count as an absolute diagnostic sign of cerebrospinal meningitis.

The differentiation of the tuberculous from other forms of meningitis by means of the character of the predominating cell found in the cerebrospinal fluid, can also not be made with positive certainty. Mononuclear lymphocytes have been observed to predominate in cases of the epidemic form of meningitis, particularly in cases which have run into the chronic stage. This is to be expected, when it is considered that the meninges react to inflammatory processes after the analogy of the serous membranes.

The only feature of the cerebrospinal fluid which remains of positive diagnostic value is the finding of the specific organism in cases of cerebrospinal meningitis. In all the forms except the tuberculous, the organism can be demonstrated in the fluid with certainty, in the early or active stages of the disease, and it is this demonstration which must be relied on for positive diagnosis. The chief difficulty in positive diagnosis is encountered in the tuberculous form, in which the tubercle bacilli cannot always be found in the cerebrospinal fluid. In these cases the differentiation of tuberculous meningitis from those diseased conditions in which the cell count is sometimes increased, with predominance of mononuclear lymphocytes, such as encephalitis, myelo-encephalitis, and the various diseases with toxic irritation of the meninges, spoken of under the title of meningismus, is very difficult. While the increase in the cell count is usually moderate, under 100 per cubic millimeter in these conditions, and is usually higher in tuberculous meningitis, yet

cases of the latter are frequent with moderate cell counts, and in some cases of meningismus the cell counts may run high. It follows that in some cases of tuberculous meningitis it is impossible to make a positive diagnosis. This should always be remembered in considering cases of reported recovery from tuberculous meningitis. Increase in the cell count, with predominance of mononuclear cells, is not sufficient for positive diagnosis. In order to make a positive diagnosis of this disease, by other means than that of autopsy, *either the tubercle bacilli must be demonstrated in the cerebrospinal fluid, or the fluid must produce tuberculosis when injected into guinea-pigs. In reported recoveries both these conditions should be fulfilled.*

It also follows that *the positive diagnosis of any form of cerebrospinal meningitis can be based only on the finding of the specific microorganism in the cerebrospinal fluid.*

Nevertheless, for ordinary clinical purposes, for the average practitioner, in presence of a definite case, certain inferences are useful. It must, however, be remembered that none of these inferences are more than those of probability, except inferences based on the finding of microorganisms.

The order in which the inferences are made during such an examination is as follows: if the fluid is cloudy, some form of cerebrospinal meningitis is present; if clear, no form of meningitis can be present, *except the tuberculous*. If the cell count is normal (under ten per cubic millimeter), no meningitis is present; if the cell count is increased (over ten per cubic millimeter and usually over 100 per cubic millimeter), some form of meningitis is present. If, with meningitis present, the predominating cell is the mononuclear lymphocyte, the evidence points toward the tuberculous form; if the predominating cell is polymorphonuclear, the evidence points toward some other form. The differentiating of these other forms depends on the finding of the specific etiologic microorganisms in the cerebrospinal fluid. The *Diplococcus intracellularis* and the influenza bacillus are recognized by their morphology and their Gram-negative staining reaction; the former also is frequently seen within the leukocytes. The pneumococcus, streptococcus, and staphylococcus are recognized by their morphology, and their Gram-positive staining reaction. The tubercle bacillus is recognized by its special staining reaction.

The chief difficulty is in distinguishing the pneumococcus from the streptococcus form, from the fact that the former frequently shows a chain formation, and its capsule is difficult to demonstrate in the cerebrospinal fluid. Nevertheless this difficulty is not so great in the cerebrospinal fluid as under some other conditions. In meningitis the streptococcus usually forms long chains, and its morphology is unmistakable;

while the pneumococcus frequently is seen in short chains, its typical form as a lance-shaped diplococcus is usually plainly evident.

The positive proof of the existence of tuberculous meningitis is also often difficult, as bacilli cannot always be found. We are obliged to depend on the increased cell count, with the predominance of lymphocytes. Where the cell count is only moderately increased, some doubt of the diagnosis will remain. Also the cell count in the cerebrospinal fluid is increased in some other conditions which, however, are not of a kind usually mistaken for tuberculous meningitis. The existence of an increased number of mononuclear cells is sufficient for ordinary clinical purposes, but if the bacilli are not found, it cannot be taken as absolute proof sufficient for scientific purposes.

THE PROGNOSIS OF CEREBROSPINAL MENINGITIS

In Table 9 is shown the outcome of the cases of cerebrospinal meningitis in my series.

TABLE 9.—THE MORTALITY OF CEREBROSPINAL MENINGITIS IN SERIES OF 142 CASES

Form	Mortality Percentage
Tuberculous	98.5
Epidemic	25
Pneumococcus	100
Streptococcus	100
Influenza	100

Tuberculous meningitis is usually regarded as an invariably fatal disease, although rare cases of recovery have been reported. In the case of recovery of the present series, the proof of the correctness of the diagnosis was, on a scientific basis, not absolutely complete. This case, together with the possibility of recovery in this disease, has been discussed in a former paper.² The two other cases of recovery, with incomplete proof of the correctness of the diagnosis, mentioned in this former report, were hospital cases and therefore not included in this present series. Whether or not there is in this disease any slight possibility of recovery, the mortality is so high that the disease may practically be regarded as invariably fatal.

In the epidemic form, the mortality given in the table represents the results of treatment with the Flexner serum, as all the cases were so treated. The mortality agrees with that of the larger series of cases reported by Flexner, and is in striking contrast with the average mortality of 75 per cent. seen before the use of the anti-serum. There were no permanent sequelæ in any of the patients who recovered in this series.

The pneumococcus and streptococcus forms may be regarded as fatal forms of cerebrospinal meningitis. The writer has found reported elsewhere no authentic cases of recovery from these forms.

The number of cases of influenza meningitis in the series is too small to give any idea of its true fatality. In all the reported cases of this form of meningitis collected by me the mortality was 50 per cent.

Cases of recovery from staphylococcus meningitis have been reported.

THE TREATMENT OF CEREBROSPINAL MENINGITIS

It is not within the scope of the present paper to discuss the general or symptomatic treatment of cerebrospinal meningitis. The only subject for discussion here is the question of the extent to which specific forms of treatment may be employed in these diseases.

The value of serotherapy in the epidemic form has been so definitely established, that no doubt can now exist that this method of treatment is indicated in all cases in which the disease is due to infection with the *Diplococcus intracellularis*. The method of administering the serum has been widely discussed in recent medical literature. I shall here call attention only to one or two facts which are sometimes forgotten. The antimeningitis serum is a specific immune serum, and is *only of value in that form of cerebrospinal meningitis which is caused by the Diplococcus intracellularis, and is of no value in any of the other forms*. The serum is of practically no value when given subcutaneously, but *must be injected directly into the spinal canal*. The reports have shown that the earlier in the course of the disease the serum is used, the better is the effect; therefore the physician should perform lumbar puncture and be prepared to use the serum *as soon as the possibility of epidemic meningitis is suspected and cannot be excluded*.

The following is a condensation of the method employed in administering the antimeningitis serum:

1. When lumbar puncture is performed in a suspicious case, be prepared to inject the serum. If the cerebrospinal fluid withdrawn is cloudy, make the injection of serum immediately and without waiting for a bacteriologic examination. The next doses of the serum are to be given only if *Diplococcus intracellularis* has been demonstrated.

2. Always withdraw as much cerebrospinal fluid as possible at each puncture and inject full doses of the serum. Thirty c.c. of serum should be injected in every instance in which this quantity of fluid or less has been removed, unless a distinctly abnormal sense of resistance in the spinal canal is encountered after as much serum has been injected as fluid has been removed. When the amount of fluid withdrawn exceeds 30 c.c., introduce a large quantity of serum—up to 45 c.c., or even more. In the very severe or fulminating cases inject from 30 to 45 c.c. of serum without reference to the quantity of fluid removed unless abnormal resistance is encountered.

3. In very severe or fulminating cases repeat the injection of serum within the twenty-four hour period, as soon as the symptoms intensify or.

when the condition remains stationary, after the lapse of the first twelve hours.

4. In cases of average severity make daily injections of full doses for four days. If diplococci persist after the fourth dose, continue the injections until they have disappeared.

5. If the subjective symptoms including fever and mental impairment persist after the diplococci have disappeared or after the four doses have been given, and improvement is not progressing, wait four days, if the condition is stationary, and then repeat the four injections. Should the symptoms have become worse before the expiration of this period, the injections should be resumed immediately.

6. In relapse, which is indicated either by reappearance of the diplococci in the cerebrospinal fluid or recrudescence of the symptoms, the four doses at twenty-four hour intervals are to be repeated and the subsequent treatment is to be conducted as for the original attack.

7. This plan of treatment is to be followed until the patient is free from symptoms, the diplococci disappear from the cerebrospinal fluid, or the chronic stage of the disease supervenes. The serum has proved of some benefit in the chronic stages in which the diplococci are still present in the meninges. When the condition of hydrocephalus has been established the injection of serum into the spinal canal promises little. It is possible that direct intraventricular injections may be of benefit in this condition.

Tuberculous meningitis has no established specific therapy. It is an interesting fact that in almost all of the few cases of reported recovery from this disease, early lumbar puncture or repeated lumbar punctures were employed. While it is impossible to establish any possible value in this method of treatment, the disease is so uniformly fatal that I believe this method of treatment, which does no harm, is worthy of trial. The disease is too rapid in its course to offer any prospect of success from vaccine therapy. I therefore believe that tuberculous meningitis should be treated with early and repeated lumbar puncture.

In pneumococcus and streptococcus meningitis the outcome is very discouraging. In epidemic meningitis, the value of serotherapy appeared to depend on the concentration with which the serum could be applied in this disease through direct injection into the spinal canal, while it was without value when given subcutaneously. The antipneumococcus and antistreptococcus sera have been more or less discredited as effective agents against their respective organisms, but they had only been used by subcutaneous injection. It occurred to me that, on the basis of analogy with the Flexner serum, these sera might also be of value when injected intradurally, and it was determined to try this method of treatment. The diagnosis cannot be made, however, at the time of the first lumbar puncture, at which time the obtaining of cloudy fluid gives a

large balance of probability in favor of the epidemic form. In most of the pneumococcus and all of the streptococcus cases, on account of this balance of probability, the Flexner serum was first injected. In the cases complicating lobar pneumonia, no antipneumococcic serum was at hand. After the examination of the cerebrospinal fluid revealed the true diagnosis, it was necessary to return with a supply of the appropriate serum. In nine of the pneumococcus cases and two of the streptococcus cases, the patients died before the appropriate serum could be given. In the three other pneumococcus cases, the patients were already moribund when the serum was given, and no favorable effect was observed. In the four streptococcus cases the patients lived several days after the serum therapy was instituted, and it was thought at this time that the progress of the disease was less rapid than before the use of the serum. In two cases there was apparent a marked diminution of the number of organisms found in the cerebrospinal fluid. There was, however, no convincing proof of good effect.

In view of the fatality of these forms, I believe that this method of treatment, on the ground of the analogy of epidemic meningitis, is worthy of further trial. The diagnosis should be made as early as possible, and the interval between the diagnostic puncture and the giving of the serum should be brief.

For influenza meningitis there is no specific therapy established. I am inclined to advocate early and repeated lumbar punctures on theoretical grounds, as a harmless method of treatment, the possible value of which may be established in the future.

In staphylococcus meningitis the evidence points toward vaccine therapy as theoretically a valuable and practically an effective method of treatment. The known great value of vaccine therapy in staphylococcus infections is a strong theoretical argument in favor of this treatment. In practice, cases of recovery from staphylococcus meningitis, under vaccine therapy, in which improvement has followed each injection of the vaccine have been reported. An homologous vaccine should be employed.

The following table shows the specific methods of treatment which in my opinion are available in the various forms of cerebrospinal meningitis, and which should be more widely tried, until further evidence proves or disproves their value.

TABLE 10.—SPECIFIC TREATMENT IN CEREBROSPINAL MENINGITIS

Form	Treatment
Tuberculous	Early and repeated lumbar puncture
Epidemic	Antimeningitis serum
Pneumococcus	Antipneumococcus serum
Streptococcus	Antistreptococcus serum
Influenza	Early and repeated lumbar puncture
Staphylococcus	Homologous vaccine

SOME INVESTIGATIONS CONCERNING THE RELATION BETWEEN CARPAL OSSIFICATION AND PHYSI- CAL AND MENTAL DEVELOPMENT*

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Dr. Rotch, of Boston, in his admirable work on "The Roentgen Ray in Pediatrics," has pointed out the need of improvement in our method of standardizing or grading growing children as to their capacity for physical and mental work. He has made the interesting and novel suggestion that the stage of ossification of the carpal bones as determined by the radiograph may be used for this purpose. If it be shown that such a test can be made and interpreted with accuracy, and that it will give an accurate index of physical and mental capacity of the subject, a very valuable contribution to the domain of preventive medicine will have been made.

The investigations described in this paper were undertaken with a view to applying the ingenious method proposed by Dr. Rotch to a few cases, and tabulating the results. These investigations have not covered the question of the relation of the development of the skeleton as a whole to physical and mental capacity, nor of the relation between carpal ossification and the rest of the skeleton.

Our work has been made possible by the Edward N. Gibbs X-ray Laboratory of the University and Bellevue Medical College, the courtesy of the Sisters of Charity and attending physicians of the New York Foundling Hospital, by the permission and cooperation of Dr. Maxwell and Dr. Crampton of the Department of Education, New York City, and by the assistance of Dr. Sheppard, superintendent, and Dr. Foster and Dr. Aldinger, in the department of physical training of the High School of Commerce, New York City, and by the aid of Dr. Goldstein and staff of the Randall's Island Children's Hospital. Among the normal children, no selection was exercised. We took all the material that we could obtain. Among the idiots we selected the most idiotic.

As stated above, we have not investigated the relation between carpal ossification and the development of the rest of the skeleton, but we have observed in more than one-third of our children so many discrepancies in development between the right and the left wrist of the same individual that we must doubt the value of using a radiograph of the wrist as an accurate index of the development of any other part of the body.

* Read before the Section on Diseases of Children of the American Medical Association, at the Sixty-First Annual Session, at St. Louis, June, 1910.

At the outset it was found exceedingly difficult to arrive at a numerical expression for the stage of carpal ossification. Up to a time this can be expressed roughly by the number of centers of ossification shown in the radiograph. But after the full number of centers has appeared the gradations from this stage to those of greater development must be expressed in the relation between the increasing calcification of the bones and the decreasing areas of the interspaces which are transparent to the x-rays. Because of the extreme irregularity in different subjects of the progress of this ossification we found it best not to attempt an expression which should fairly represent the degree or stage of carpal ossification, but to grade the radiographs in numerical order from that of least to that of greatest development.

In the investigation which we have made radiographs have been taken of both wrists in about 200 subjects, varying in age from infants to young men, and in mental capacity from idiots and cretins to the exceptionally brilliant high school boy. Age, height, weight and mentality have been noted, and in the high school boys exercise and stage of pubescence have been added. Photographs have been taken of many of the cases. They may be divided into three main groups: (1) children; (2) high school boys; (3) idiots.

Figure 14 shows the ages of all the children expressed in vertical lines drawn to scale, beginning with an infant 1 year, 1 month, and 10 days old, and ending with a child of 14 years, 5 months, and 20 days. The children are graded in numerical order from left to right, according to their carpal development. It is seen that the child whose wrist is twelfth in carpal development is of greater age than all others up to the sixty-seventh. Wrist 73 is younger in years than Wrist 10. Only after Wrist 118 do all the ages exceed that of Wrist 12. It is seen that only in a very general way does the age increase with carpal development.

Figure 15 is a chart showing height, which, like age, presents only a general increase with carpal ossification. The shortest child is an achondroplasiac, and is forty-seventh according to its carpal classification.

Figure 16 presents between weight and carpal development the same general correlation. The child of the least developed wrist, No. 1, exceeds in weight Child 78. Child 41 in wrist exceeds all others in weight up to No. 79, and only after No. 95 do all weights exceed No. 41.

In Figure 17 the radiographs of the children's wrists are still graded in numerical order, but are grouped to indicate similarity in development, and are lettered according to Dr. Rotch's classification. Where two letters are used the wrists appeared so indefinite as to belong in either or both classes. Age, height, weight and mental ability are recorded. Seven degrees of mentality have been used. 1 for idiotic; $1\frac{1}{2}$ for very dull; 2 for dull; 3 for fair; 4 for bright; 5 for very bright; and 6 for exceptionally bright. Four children, the brightest of all, have been



Fig. 1.—Radiograph of wrists and hands of Augustine A., aged 14 months. (12453 A.) Epiphysis of left thumb present; epiphysis of right thumb absent.



Fig. 2.—Radiograph of wrists and hands of Walter M. (12437), aged 4 years, 4 months and 8 days. Three centers of ossification in left hand; two in right.



Fig. 3.—Radiograph of wrists and hands of Victor S. (12403), aged 4 years, 7 months and 15 days. Two centers of ossification in left hand; three in right.



Fig. 4. Radiograph of wrists and hands of Frances B. (12414), aged 5 years, 11 months, and 16 days. Three centers of ossification in left hand; four in right.



Fig. 5.—Radiograph of wrists and hands of Michael H. (12451), aged 3 years, 3 months and 8 days. Three centers of ossification in left hand, four in right. No epiphysis of thumb in either.



Fig. 6.—Radiograph of wrists and hands of James F. (12450 A), aged 4 years, and 3 days. Four centers of ossification in left hand, three in right.



Fig. 7.—Radiograph of wrists and hands of Alice M. (12419), aged 3 years, 10 months and 22 days. Three centers of ossification in left hand, four in right.



Fig. 8.—Radiograph of wrists and hands of John E. (12410), aged 2 years, 4 months and 4 days. Five centers of ossification in left hand, four in right.



Fig. 9.—Radiograph of wrists and hands of Mary B. (12388), aged 6 years, 6 months and 25 days. Six centers of ossification in left hand, five in right.

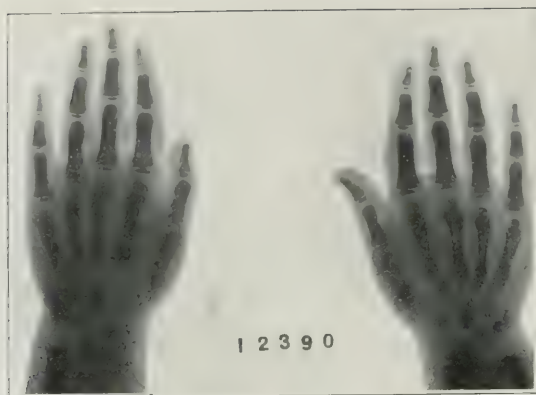


Fig. 10.—Radiograph of wrists and hands of Bessie D. (12390), aged 5 years and 1 day. Four centers of ossification in left hand, with large epiphysis of thumb; five in right with sixth just appearing.



Fig. 11.—Radiograph of wrists and hands of Marjorie K. (12400), aged 5 years, 6 months and 5 days. Seven centers of ossification in left hand, six in right.



Fig. 12.—Radiograph of wrists and hands of Sophia W. (12398), aged 5 years, 2 months and 12 days. Seven centers of ossification in left hand and no epiphysis of ulna; in right, six centers with seventh just appearing and epiphysis of ulna present.

marked 7. This estimate was made up from the opinion of a nurse well acquainted with the children, their kindergarten teachers, and our own observations. Where age only is shown, other data could not be obtained. The children of Classes A and A-B are healthy infants. The first walks: the second, 6 months older, does not walk. The first wrist of Class B, the youngest in carpal development, is of a child which, except for one other, is the oldest in years of the entire class of seventeen. It is the tallest, the heaviest and the best mentally. In the second group of Class



Fig. 13. Radiograph of wrists and hands of Frank O. (12412), aged 7 years, 4 months and 10 days. Six centers of ossification in left hand; seven in right.

TABLE 1.—SHOWING CARPAL DEVELOPMENT IN CONNECTION WITH AGE, HEIGHT, WEIGHT AND MENTAL DEVELOPMENT

Group	Age	Height	Weight	Mind
1.....	—	—	—	—
2.....	+	+	—	—
3.....	+	+	+	+
4.....	+	+	+	—
5.....	+	=	—	—
6.....	—	—	—	=
7.....	—	—	—	—
8.....	=	+	+	+
9.....	+	+	—	=
10.....	+	=	+	—
11.....	—	—	—	—
12.....	—	—	—	+
13.....	+	+	+	—
14.....	+	+	+	—
15.....	—	+	+	—
16.....	+	+	—	—
17.....	+	+	+	+
18.....	+	+	+	—
19.....	+	=	—	—
20.....	+	+	+	=
21.....	+	+	+	—
22.....	+	+	+	=
23.....	+	—	+	—
24.....	+	+	+	+
25.....	+	+	+	=

B, the youngest child, aged 2 years, 6 months and 15 days, is very bright, while the oldest, 6 years, 7 months and 29 days, is very dull, while their wrists are very similar in stage of development, being only one number apart. In Class C the wrists of least and greatest development are of children with the same degree of mentality. The former is the older in years. In Class D the same is true as to mentality, with the opposite as to age. The youngest child in this class is 2 years, 2 months and 2 days, while the oldest is 7 years and 29 days. The youngest of fair intelligence; the oldest very bright. In Class G the first is an idiot, while the second and third following are very bright.

In all there are twenty-five groups of two or more children in each. The wrists increase in development from left to right. A comparison of the age, height, weight and mind of the first and last child in each group, these children representing extremes of carpal development, may be shown thus: where the age, height, weight or mind of the last child is greater than that of the first child in the same group a plus sign (+) is used, and the increase is in accord with carpal development; where the last is less than the first a minus sign (—) is used and the decrease is contrary to the carpal development; where the last and first are equal a sign of equality (=) is used, but the result is still out of accord with carpal development, as this increases from first to last.

From the accompanying table, a comparison between the last child and the first child of each group, it will be seen that eighteen of the twenty-five groups increase in age with carpal development; seventeen in height and fifteen in weight. In mentality fifteen of twenty-five decrease with increase in carpal development; five remain the same, or in four fifths of these groups the child of least carpal development equals or exceeds in mental ability the child of greatest carpal development.

Our second main group of cases (Fig. 18) is composed of eighty-seven high school boys who were chosen with the purpose of learning the relation between the stages of carpal ossification and the stages of pubescence. Age, height, weight, scholarship and exercise have been noted. These data were taken from charts prepared by Dr. C. Ward Crampton, of the Department of Education, New York City, in his valuable work on "Physiologic Age." He has used the appearance of pubic hair as an index of the stage of puberty; e. g., N indicates that no hair has yet appeared and the boy is pre-pubescent; AP that the hair is just appearing and the boy is in the first stage of pubescence; ST that the hairs have become straight and represent a later stage; C that the hair has become curly, and is used with exponents to express still further stages of pubescence up to C5, which indicates that the growth of pubic hair has become complete, and the subject has passed all stages of pubescence,

A
G
E



Fig. 14.—Chart of ages of all children expressed in vertical lines drawn to scale.

and has become a postpubescent. The boys chosen by us are as follows: 24 N, 6 AP, 8 ST, 9 C1, 6 C2, 5 C3, 6 C4, and 23 C5. As there should be the greatest difference between prepubescents and postpubescents, the larger number of boys were chosen from these. The wrists were carefully compared and arranged in order from that of the least to that of the greatest carpal development.

The stage of pubescence was then noted together with the height, weight, etc. It is seen that the carpal development increases in general with the stages of pubescence, that most of the N boys are at the begin-

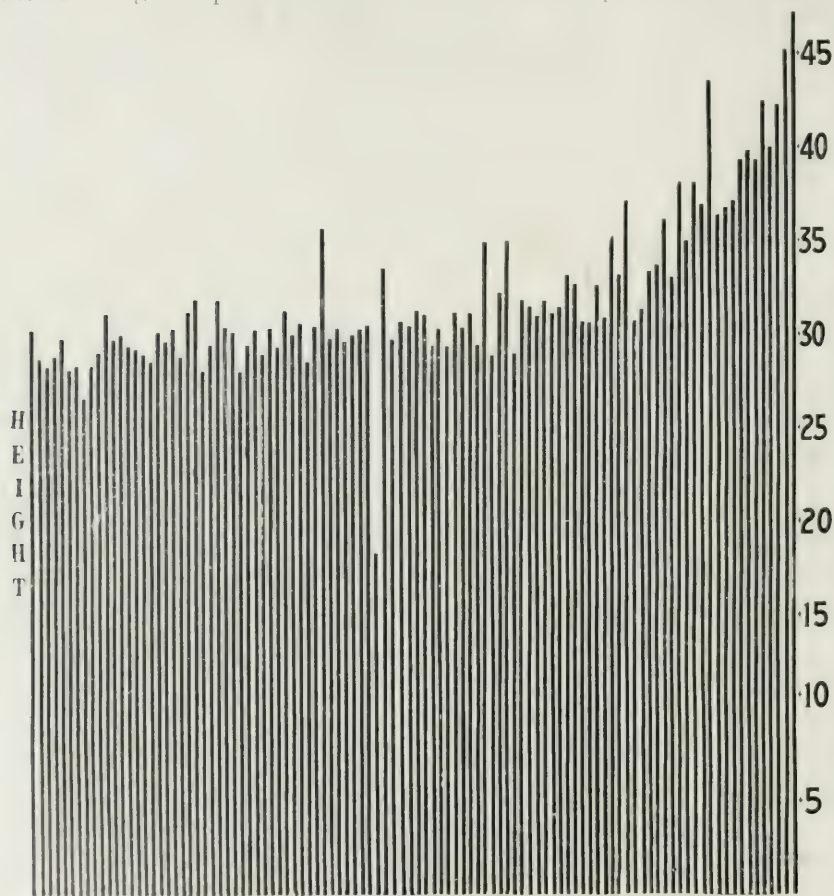


Fig. 15. Chart showing height of all the children expressed in vertical lines.

ning while the C5 men are toward the end of the chart. There are, however, so many exceptions that carpal ossification, in this limited number of cases at least, does not accurately correspond with the stage of pubescence.

Photographs were taken of the boys grouped according to their stage of pubescence or the "physiologic age" of Crampton, that we might note

their general appearance when so grouped and compare it in our minds with what would be the case were they grouped according to their stage of carpal ossification. A difference in appearance is noticeable between all groups, but most strikingly between group X and group C5.

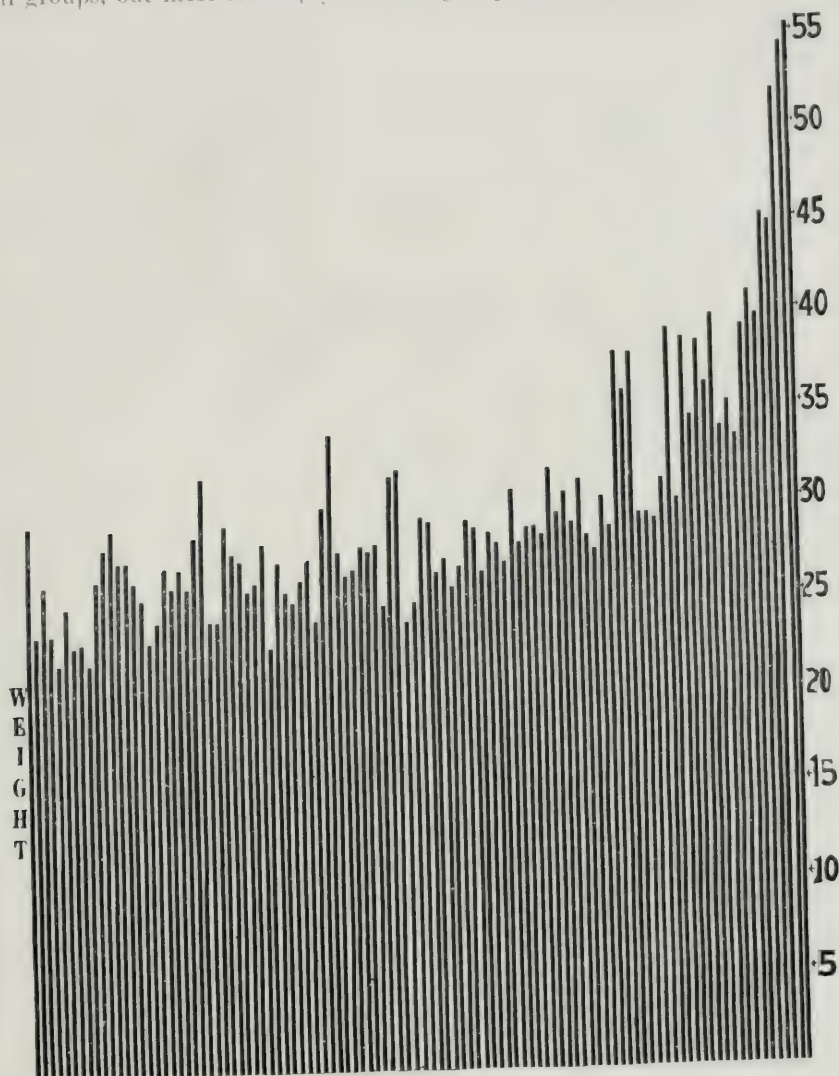


Fig. 16. Chart showing weight of all children expressed in vertical lines.

Ages are drawn as beginning at 12 years, heights from 100 centimeters, weights are indicated in full. Scholarship is represented by an average of all marks during the first term, and are drawn in full. "X" indicates that the boy has taken athletic exercise before entrance, "O"

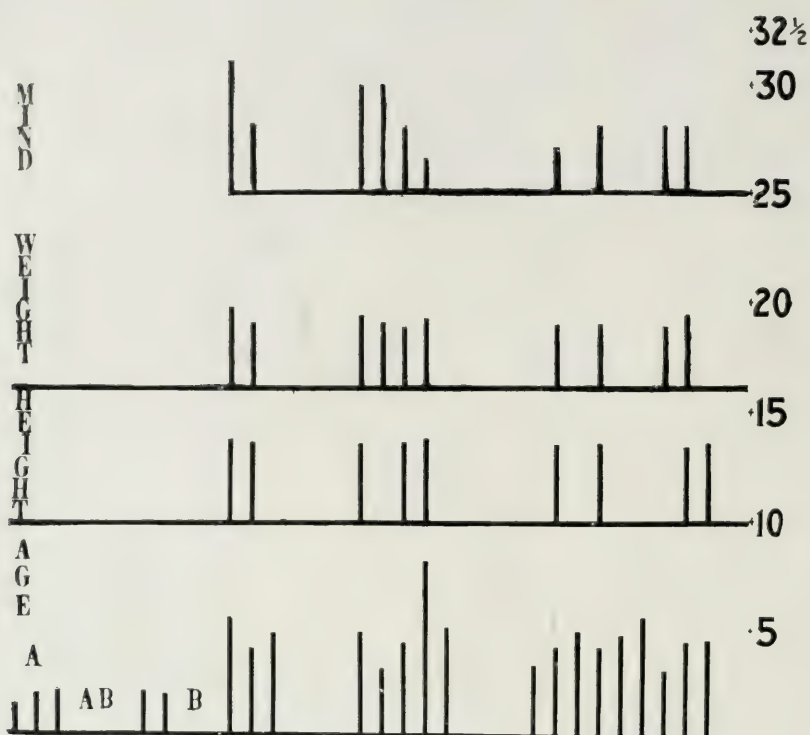


Fig. 17.—Section 1.

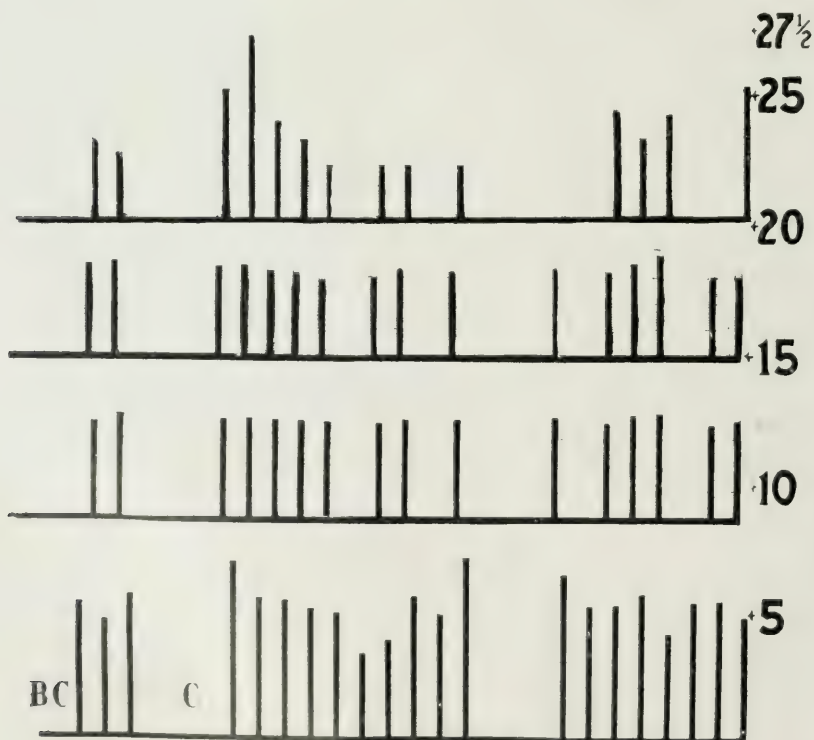


Fig. 17.—Section 2.

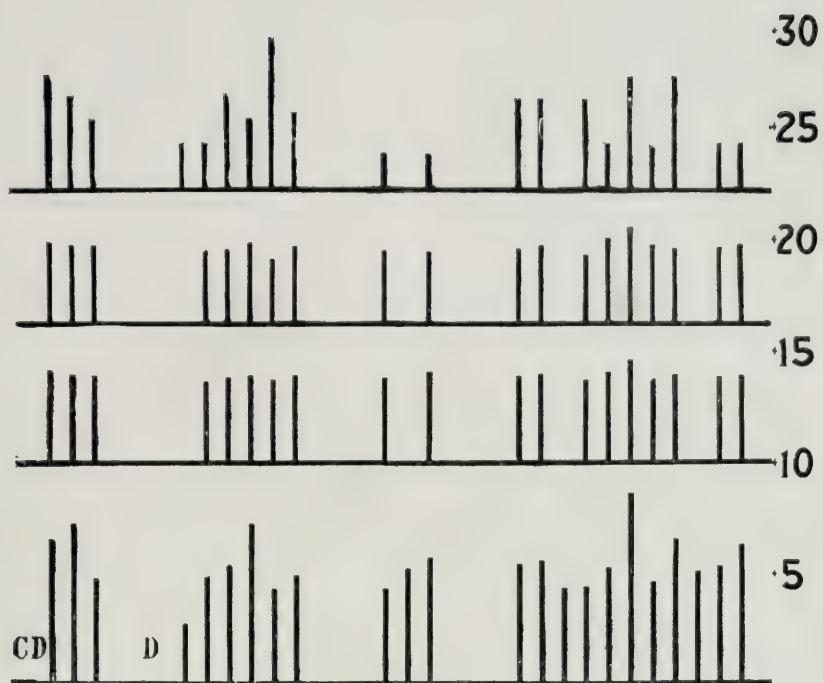


Fig. 17.—Section 3.

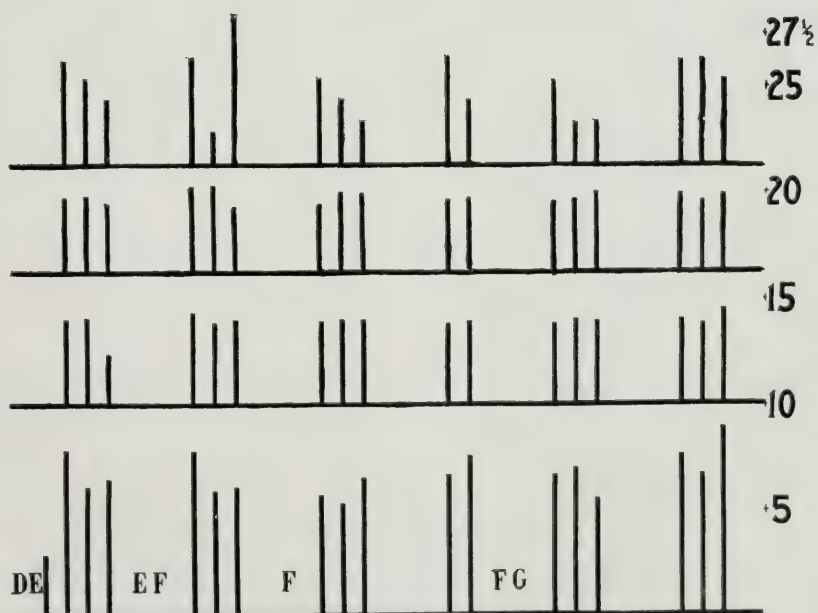


Fig. 17.—Section 4.

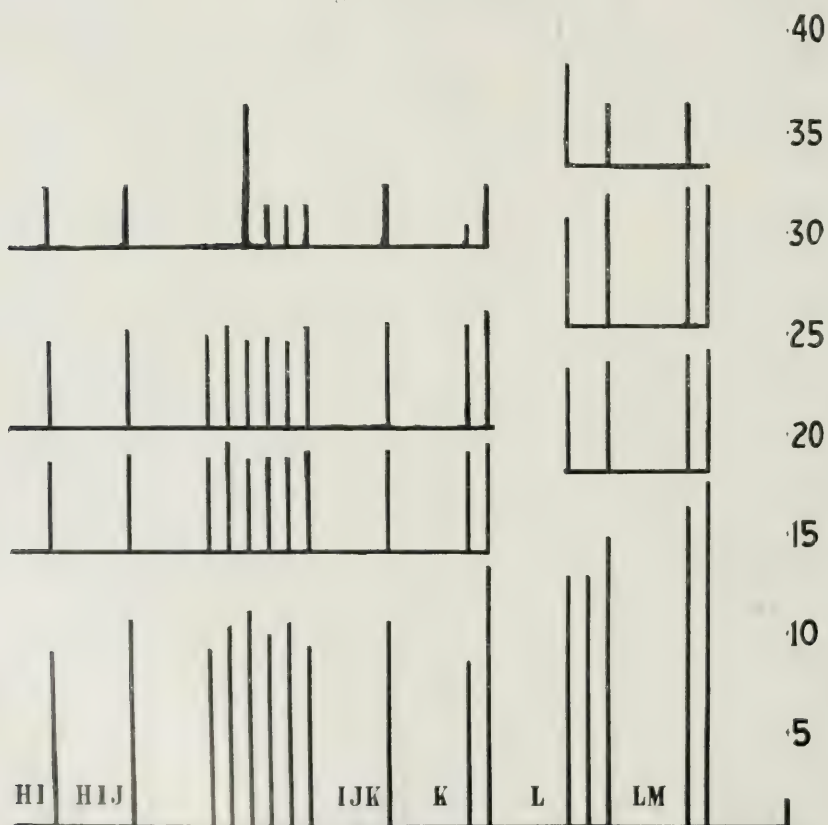
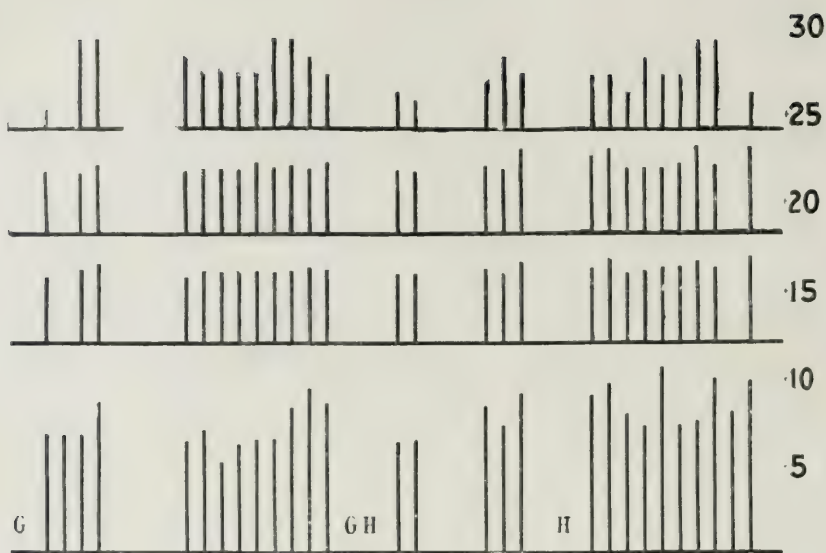
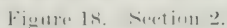
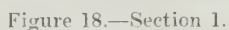


Fig. 17. Section 6. Chart of mental development, weight, height and age of children grouped to indicate similarity in development and according to Rotch's classification.



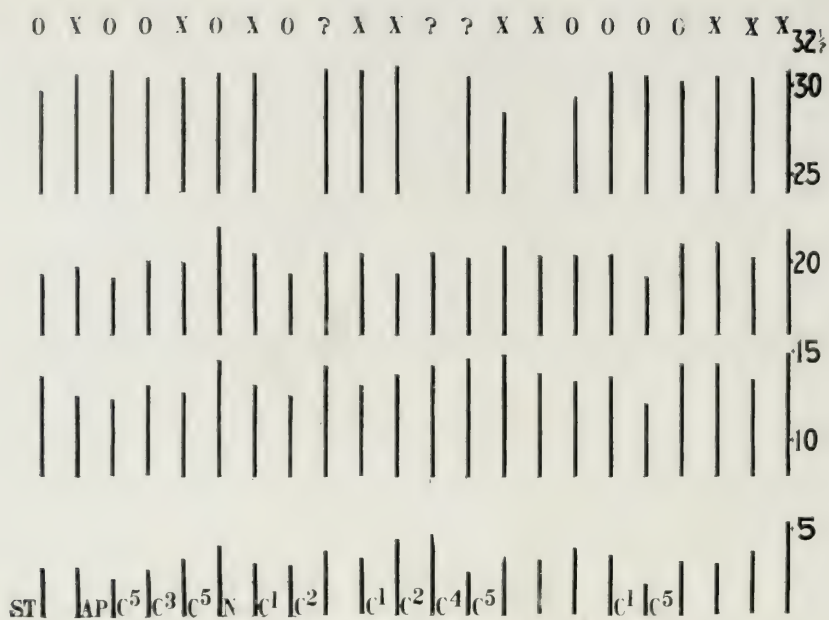


Figure 18.—Section 3.

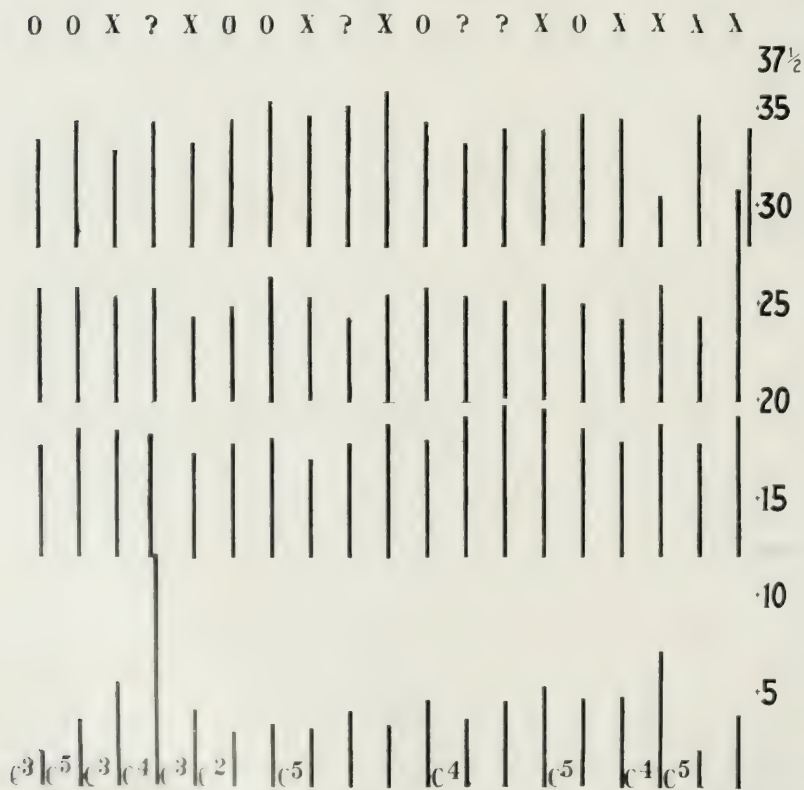


Fig. 18.—Section 4. Chart of relation between stages of carpal ossification and stages of pubescence.

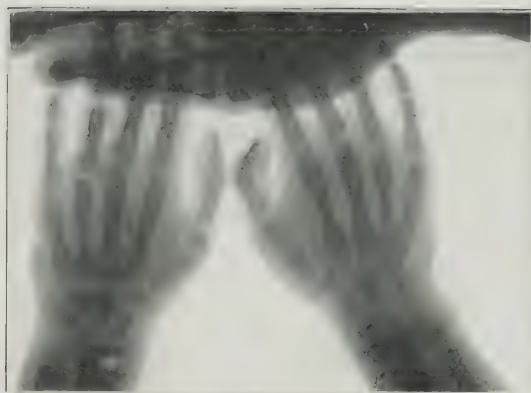


Fig. 19.—Radiograph of wrists and hands of Helen F. (I 3), aged 5, idiotic; has enlarged lymph-nodes and exaggerated patellar reflexes; walks with difficulty, cannot feed herself.

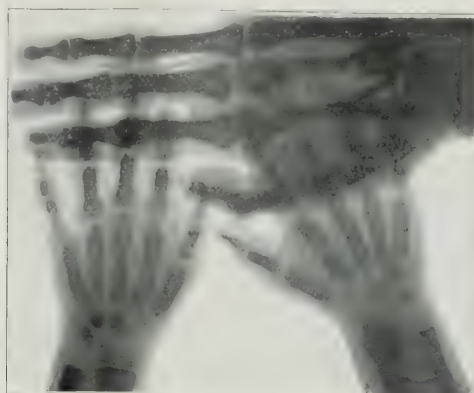


Fig. 20.—Radiograph of wrists and hands of Frida A. (I 5), aged 5; Mongolian idiot; has poor circulation; does not dress or feed herself; is of unclean habits.



Fig. 21.—Radiograph of wrists and hands of Sadie B. (12394), normal child, aged 5 years, 7 months and 5 days; of bright mentality. In carpal development both idiots (Figs. 19 and 20) exceed the normal child. While the younger idiot has smaller centers, it has in advance of the normal child the epiphysis of the ulna.



Fig. 22.—Photographs of Helen F. and Frida A. whose carpal development was shown in figures 19 and 20.



Fig. 23.—Radiograph of wrists and hands of Lulu B. (I 9), aged 9 years and 6 months; feeble-minded; dresses and feeds herself.



Fig. 24.—Radiograph of wrists and hands of Mary C. (12381), very bright normal child, aged 9 years, 2 months and 10 days. The idiot's wrist (Fig. 23) is in advance of that of the normal child.

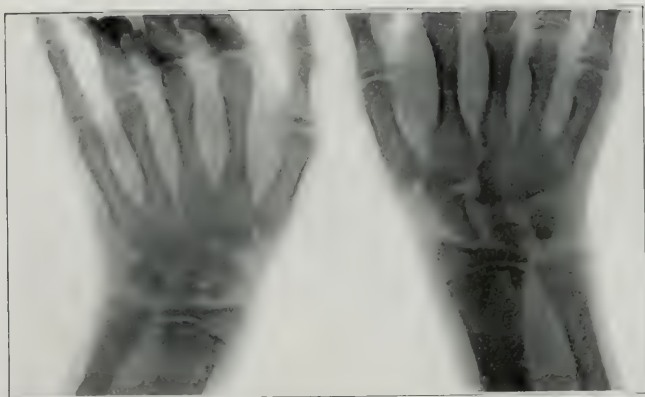


Fig. 25.—Radiograph of wrists and hands of Elsie O. (11), aged 12: microcephalic idiot; does not dress or feed herself; is of unclean habits; jabbbers constantly.



Fig. 26.—Portraits of Lulu B. and Elsie O., whose wrists and hands are shown in Figures 23 and 25.



Fig. 27.—Radiograph of wrists and hands of Mary C. (4747), normal child of fair mentality, aged 12 years, 2 months and 9 days. The normal child somewhat exceeds the idiot (Fig. 25).

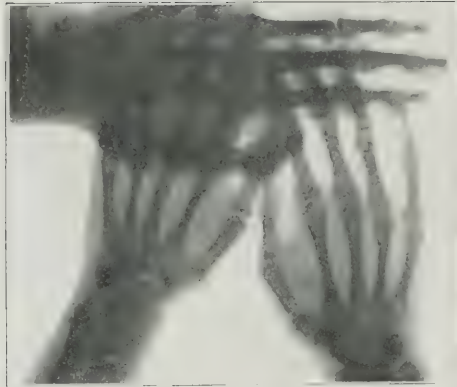


Fig. 28.—Radiograph of wrists and hands of Bertha L. (I 11), aged 14, microcephalic idiot; does not feed or dress herself or answer to name; is of fairly clean habits. These wrists are considerably in advance of those of M. C. (Fig. 27).



Fig. 29.—Radiograph of wrists and hands of Florence B. (I 7), imbecile aged 22, who dresses and feeds herself. These wrists show still further advance.



Fig. 30. Portraits of Bertha L. and Florence B. whose wrists and hands are shown in Figures 28 and 29.



Fig. 31.—Radiograph of wrists and hands of David W. (I 12), a blind idiot, aged 6, who does not dress or feed himself; is of unclean habits. .



Fig. 32.—Radiograph of wrists and hands of Sylvester B. (12416), very bright normal child, aged 7 years, 1 month and 10 days. The idiot's carpal ossification (Fig. 31) is far in advance of the normal child.



Fig. 33.—Portraits of David W. and Benny L., whose wrist developments are shown in Figures 31 and 43.



Fig. 34.—Radiograph of wrists and hands of Arthur B. (I 6), idiot, aged 14, who is clean, feeds and dresses himself, marches and folds paper, but does not answer to name and cannot learn the alphabet.



Fig. 35.—Radiograph of wrists and hands of normal boy (922) aged 14 years, 11 months and 22 days, whose school average is 74.5 per cent. The idiot's wrist (Fig. 34) is the further developed.

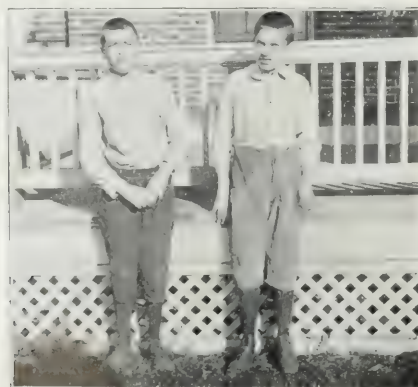


Fig. 36.—Portraits of Arthur B. and Charles B., whose wrists and hands are shown in Figures 34 and 40.



Fig. 37.—Radiographs of wrists and hands of Isadore I. (I 4), an idiot aged 15, who feeds himself and marches only; has undescended testes.

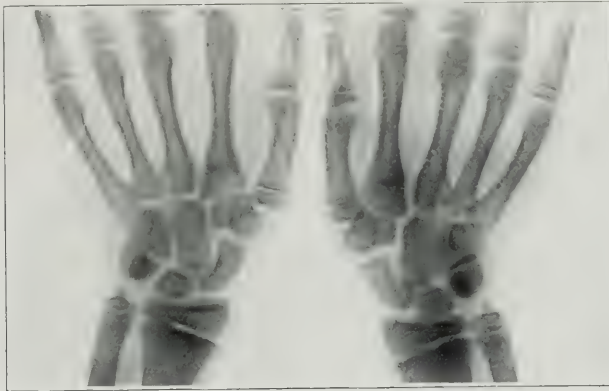


Fig. 38.—Radiograph of wrists and hands of normal boy (912 cl), aged 15 years, 9 months and 13 days; school average 52.6 per cent. The idiot (Fig. 37) exceeds the normal boy.



Fig. 39.—Photographs of Isadore L. and Samuel S., whose wrists and hands are shown in Figures 37 and 41.

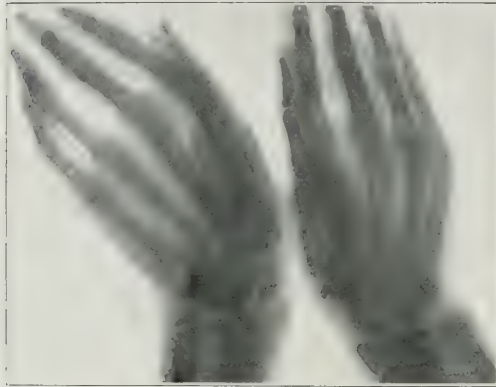


Fig. 40.—Radiograph of wrists and hands of Charles B. (I 8) blind idiot aged 17, who marches, folds paper, sews buttons, does raffia work but does not answer to his name.



Fig. 41.—Radiograph of wrists and hands of Samuel S. (I 10), blind idiot aged 18, who is unclean and does not answer to name or feed himself.



Fig. 42.—Radiograph of wrists and hands of normal boy (459 C 4), aged 17 years, 11 months and 19 days; school average 96.5 per cent. Normal boy seems to exceed both the younger and older idiots (Figs. 40 and 41).

that no exercise has been taken, and “?” that no information was obtainable.

The third group of cases is of five male and six female idiots and one male cretin. Their carpal development is compared with that of normal children of the same sex and as near the same age as possible.

The idiot girls, Helen F. and Frida A., of about the same age, are nearest alike in height and in carpal ossification. Lulu B., aged $9\frac{1}{2}$



Fig. 43.—Radiograph of wrists and hands of Benny L. (I 2), a cretin aged 21; fairly intelligent midget.



Fig. 44.—Radiograph of wrists and hands of normal boy (799 C 4), aged 22 years, 1 month and 21 days; school average 65.5 per cent. The normal boy exceeds the cretin (Fig. 43).

years, and Elsie O., aged 12, present a like similarity. The same is true of Bertha L., aged 14, and Florence B., aged 22.

Of the boys, the oldest, Benny L., a dwarf cretin 21 years old, and the youngest, David W., aged 6, are nearest alike in height and also in carpal

development. This relation between height and carpal ossification holds good, regardless of age, between the others, namely, Samuel S., aged 18, and Isadore I., aged 15, and between Arthur B., aged 15, and Charles B., aged 17.

We have in the course of our work examined children at monthly intervals, and have found in some cases an advance in carpal development, e. g., a new center appearing, while in other cases no advance has been present.

In view of the general correlation between height and carpal development, as seen in Figure 15 and as illustrated by the idiots' radiographs and photographs, successive examinations of the carpus might, when considered with other factors such as sex, race, heredity, age, height and weight, serve as an aid to indicate the rapidity of skeletal development and the possible future height of the child.

From this limited investigation we are led to believe that the ossification of the one wrist of an individual is not an exact index of the ossification of the other wrist, and therefore it seems probable that the same inexact relation exists between the wrist and the remainder of the skeleton. Age, height and weight increase in general with advance in carpal ossification, but with many exceptions among both sexes. It would be impractical at least to regulate the mode of life of these children according to this classification alone, e. g., Class B includes a very bright child, 2 years, 6 months and 15 days old, and a very dull child of 6 years, 7 months and 29 days; Class D includes a child of fair intelligence, 2 years, 2 months and 2 days old, with a very bright child of 7 years and 29 days. We can find no relation between degree of carpal development and quality of mind. Some idiots are as far advanced in carpal ossification as some normal children of good mentality and similar chronologic age. The relation between the stages of puberty and those of carpal ossification is too indefinite to warrant the latter's use as an index of physiologic development. And, finally, though carpal development alone is not an exact index, still when observed at intervals, and considered with other factors, it may become an aid in estimating the rapidity of growth of the skeleton in children.

We believe with Dr. Rotch that closer attention should be paid by the medical profession to the regulation of physical and mental tasks more in accordance with the individual child's capacity, and hope that development of the ossification centers of the skeleton, as brought before us by Dr. Rotch, though not an index in itself, may become a factor toward this result.

FREQUENCY AND SIGNIFICANCE OF ALBUMIN IN THE URINES OF NORMAL CHILDREN

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For some years past we have been much impressed by the frequency with which albumin, varying in amounts from very slight to marked traces, has been reported present in the urines of children we have seen in private practice. In these children we have been unable to detect abnormalities which we considered sufficient to account for the albumin.

Stimulated by these findings, we undertook the studies set forth in this paper and in presenting them we shall not undertake a discussion of the extensive and valuable work which has been done on the albuminurias, but merely state the results of our own work. Our purpose has been to determine the frequency of occurrence of albuminuria, and, if possible, to throw some light on the cause of this frequency. To this end we have made examinations of the urines of 124 presumably normal children taking samples at frequent intervals on the same day, and over a period of days, as well as samples covering the full twenty-four-hour period.

In carrying out this work, we have considered it advisable to make complete examinations of the urine and to use tests easy of application and at the same time reliable.

The following is an outline of our routine procedure: In each sample of urine, we determined the color, the appearance, the specific gravity, the reaction (in twenty-four-hour specimens, the total acidity), the presence or absence of albumin, sugar, acetone, diacetic acid, indican, urobilinogen, and phenol; and microscopically, the presence or absence of cells, casts, cylindroids, and crystals.

TESTS USED

For the determination of the specific gravity, we used Squibb's urinometer, graduated to 25 C.; for the reaction, litmus paper; for albumin (all specimens having been made clear either by filtering or by the addition of magnesia and filtration) Heller's nitric acid test, observed at intervals of one, three, and five minutes, the heat test, observing it immediately as well as after the addition of acetic acid, the potassium ferrocyanid test, contrasting it with the cold urine to which acetic acid had

been added, and the acetic acid test, in which a few drops of 50 per cent. acetic acid were added to the untreated urine. In each of these tests, in addition to the contrasts made above, comparisons were made with the untreated urine and always against a black background. When the specific gravity was 1.024 or over the urine was diluted and both samples tested. For sugar we used Fehling's test; for acetone, Lange's test, controlled by Stock's test; for diacetic acid, Gerhardt's test; for indican, Obermayer's test; for urobilinogen, the dimethylamidobenzaldehyd reaction; and for phenol, the urine was treated with 25 per cent. sulphuric acid and the distillate with bromin water. In the microscopic examination, two slides from the centrifugalized sediment were studied.

The routine examination for bodies other than albumin was made in order to determine whether, if present, they might have some bearing on the occurrence of the albumin, or indicate some abnormal condition to which it could be attributed.

With the same idea in view, we examined the stools in certain groups of cases amounting to about one-third the total number. This included the form, color, odor, reaction, and evidences of fermentation and the presence of mucus and undigested food particles; and under the microscope the presence of starch, neutral fats, soaps, and crystals.

SOURCE OF MATERIAL

Four hundred and forty-five specimens of urine were examined. These were obtained from 124 children, ranging in age from 18 months to 14 years. For convenience of consideration we have divided these latter into four groups as follows:

1. Children obtained from a number of different sources.
2. Children obtained from the orthopedic ward of the hospital of the University of Pennsylvania, suffering from congenital or acquired deformities (other than tuberculous).
3. Children from the Baptist Orphanage of Philadelphia.
4. A group of three children, whose urines were examined practically every day for several weeks.

SPECIMENS USED

In the majority of the children in Group 1, only morning samples were examined; in a smaller number, both morning and evening.

In Group 2, consisting of thirty-one cases, only morning examinations were made in twenty-four, both morning and evening in thirteen, and morning, noon, and evening for two successive days in three cases. In the last case of this group, for reasons to be considered later, examinations were made for six successive days. The first sample was taken immediately on waking, the second at 9 a. m., and the others at noon and evening. On the first day the child was up and about the ward and on the regular hospital diet. On the second day he was in bed on the same diet;

on the third day the conditions were the same. On the fourth day he was again up and about on the hospital diet. On the fifth day he was up and about on an exclusive milk diet; on the sixth day he was in bed on a milk diet.

Group 3 consisted of thirty-six institutional children. We are quite aware that the normality of such children may be questioned, but they are included because, aside from being well-nourished and free of organic diseases, the conditions under which they live are entirely normal. The home is constructed on the cottage plan, each cottage being under the direction of a house-mother who has charge of about twenty-five children. The food supplied them is not only adequate, digestible, and well-balanced, but also admirably prepared. The sleeping-apartments are spacious, well ventilated and perfectly clean. The play-ground consists of an enclosure of about six acres. Aside from this the children are still further detached from the ordinary institutional environment by the fact that they receive their education in the public schools.

During the period of examination the usual routine of life was followed, except that the children were kept from school. They were studied in groups of three, each group being under the constant supervision of a trained nurse in order to insure the proper collection of specimens. The following routine was then followed:

A complete physical examination was made to exclude acute and chronic diseases and defects of development. The specimens were collected immediately on rising, and thereafter at 9 a. m., 12 noon, and 6 p. m. In addition the total quantity for twenty-four hours was taken. The body temperatures were recorded every fourth hour during the day. The pulse rate and the blood-pressure (by Stanton's apparatus) were determined in the upright and recumbent postures on the day that the samples were collected; and a sample of the stools from each case was taken.

In Group 4, ninety-five examinations were made. The specimens represented the morning urine for a portion of the time, the mid-day for another, and both the morning and evening for the remainder. On two occasions, separated by some days, the twenty-four-hour quantity was collected and examined.

RESULTS OF THE EXAMINATION

There has been wide variation in the *specific gravity* of the urine voided at different periods of the same day. In the majority of instances it has been higher in that voided immediately on rising and in the urine voided at the end of the day, but this has not been constant. In the twenty-four-hour specimens (forty-two in number) the specific gravity has been much higher than the averages given in text-books and monographs for children whose ages were the same as those we have studied. The specific gravity bore no definite relationship to the amount of urine voided. Thus in a child voiding but 475 c.c. in twenty-four hours, the

TABLE 1. CHILDREN OF GROUP I OBTAINED FROM DIFFERENT SOURCES*

Name	Sex	Age Years	Date†	Color‡	Spec. Grav.	Albumin§	Indican, Urobilinogen, Phenol	Crystals Casts, Cylindroids,
J. C.	M	6	12/7/09 a. m.	L. A. . .	1010	S. T. nucleo	Urobilin; phenol	None
M. J.	F	3	1/22/09 a. m.	L. A. . .	1018	V. S. T. nucleo	None	Hyaline; cylindroid
J. C.	M	10	1/24/10 a. m.	A. . . .	1021	V. S. T. nucleo	Phenol	Hyaline; cylindroid
J. K.	F	6	1/19/10 a. m.	L. A. . .	1018	None	Phenol	Uric acid
P.	M	7	1/28/10 a. m.	A. . . .	1016	V. S. T. nucleo	None	None
M. E.	F	12	2/20/10 a. m.	L. A. . .	1021	V. S. T. nucleo	None	None
L. E.	M	4	11/29/09 a. m.	L. A. . .	1010	V. S. T. nucleo	Phenol	Cylindroid
L. E.	M	6	11/23/09 a. m.	A. . . .	1036	S. T. nucleo	Urobilin	Amorph. urates
J. L.	M	1½	11/15/09 a. m.	L. A. . .	1022	S. T. serum	Urobilin	Calc. oxalate; am- mon. urates
S. C.	F	10	12/1/09 a. m.	L. A. . .	1020	V. S. T. nucleo	None	None
H. C.	F	10	1/22/10 a. m.	L. A. . .	1018	T. nucleo; T. serum	None	None
R. W.	F	6	11/29/09 a. m.	L. A. . .	1020	V. S. T. nucleo	Phenol	Calc. oxalate
H. C.	M	4	11/29/09 a. m.	L. A. . .	1018	V. S. T. nucleo	None	None
C. W.	M	8	11/29/09 a. m.	P. . . .	1018	None	Urobilin; phenol	None
S. W.	F	12	11/29/09 a. m.	P. . . .	1015	V. S. T. nucleo	Phenol	Amorph. urates
S. R.	F	3	11/23/09 a. m.	L. A. . .	1027	V. S. T. nucleo	None	None
S. R.	F	11	11/9/09 a. m.	L. A. . .	1022	V. S. T. nucleo	Indican; phenol	None
L. M. C.	M	11	11/9/09 a. m.	L. A. . .	1016	V. S. T. nucleo	None	None
A. H.	M	8	11/10/09 a. m.	L. A. . .	1016	V. S. T. nucleo	None	None
E. B.	F	10	11/3/09 a. m.	A. . . .	1026	S. T. nucleo; T. serum	Urobilin	None
E. W.	F	6	12/17/09 a. m.	L. A. . .	1029	V. S. T. nucleo	None	Hyaline; cylindroid
T. C.	M	6	11/8/09 a. m.	P. . . .	1008	V. S. T. nucleo	None	None
T. C.	M	6	11/11/09 a. m.	L. A. . .	1016	None	Indican; Urobilin- lin.; phenol	None
H. T.	F	14	2/10/10 a. m.	L. A. . .	1020	V. S. T. nucleo; S. T. serum	Urobilin	Calc. oxalate
M. S.	F	10	2/10/10 a. m.	A. . . .	1020	T. nucleo	None	Uric acid
E. H.	M	2	3/11/10 a. m.	A. . . .	1030	S. T. nucleo	None	Hyaline; cylindroid; Calc. oxalate
R. J.	M	9	3/11/10 a. m.	L. A. . .	1027	S. T. nucleo	Urobilin	Calc. oxalate
F. E.	F	6	3/2/10 a. m.	L. A. . .	1027	None	None	None
F. E.	F	6	3/11/10 a. m.	L. A. . .	1020	V. S. T. nucleo	None	Hyaline; cylindroid
L. E.	M	9	3/11/10 a. m.	L. A. . .	1020	V. S. T. nucleo	None	Uric acid
T. C.	M	2½	12/8/09 a. m.	A. . . .	1020	None	None	None
S.	M	5	12/8/09 a. m.	L. A. . .	1010	V. S. T. nucleo	Indican; phenol	None
W. C.	M	9	12/10/09 a. m.	L. A. . .	1010	V. S. T. nucleo	None	None
L. B.	F	9	12/10/09 a. m.	A. . . .	1013	None	None	None
E. C.	F	14	12/20/09 a. m.	L. A. . .	1014	V. S. T. nucleo	Phenol	Hyaline; cylindroid
R. C.	F	4	12/20/09 a. m.	L. A. . .	1015	V. S. T. nucleo	None	Uric acid
R. W.	F	7	12/20/09 a. m.	L. A. . .	1027	None	None	None
M. C.	F	10	12/20/09 a. m.	L. A. . .	1022	S. T. nucleo; S. T. serum	None	Amorph. urates
J.	F	1½	12/30/09 a. m.	L. A. . .	1024	None	Urobilin	None
J.	F	1½	11/26/09 a. m.	L. A. . .	1022	V. S. T. nucleo	None	Calc. oxalate
R. S.	F	1½	11/29/09 a. m.	A. . . .	1020	V. S. T. nucleo	None	None
R. S.	F	1½	12/2/09 a. m.	P. . . .	1022	V. S. T. nucleo	None	None
R. S.	F	1½	12/10/10 a. m.	L. A. . .	1024	V. S. T. nucleo	None	None
R. S.	F	1½	2/14/10 a. m.	L. A. . .	1017	V. S. T. nucleo	None	None
J. K.	F	10	11/3/09 a. m.	L. A. . .	1018	V. S. T. nucleo; V. S. T. serum	None	Calc. oxalate

J. K.	F	10	11/16/09 a. m.	L. A. . .	1016	V. S. T. nucleo; V. S. T. serum	Indican; phenol	None
J. K.	F	10	12/20/09 a. m.	L. A. . .	1024	V. S. T. nucleo	Urobilin	Calc. oxalate
J. K.	F	10	2/ 6 10 a. m.	L. A. . .	1026	V. S. T. nucleo	None	Hyaline; cylindroid
A. R.	F	8	1/ 19, 10 a. m.	L. A. . .	1020	T. nucleo; T. serum	None	Hyaline; cylindroid
A. R.	F	8	1 21/10 a. m.	L. A. . .	1021	V. S. T. nucleo	Phenol	None
A. R.	F	8	1/ 28, 10 a. m.	L. A. . . .	1020	T. nucleo; T. serum	Urobilin	None
A. R.	F	8	2/ 3/10 a. m.	L. A. . .	1016	S. T. nucleo;	Phenol	None
A. R.	F	8	2/ 4/10 a. m.	L. A. . .	1020	V. S. T. nucleo	Phenol	None
J. B.	F	10	3/ 11/10 a. m.	L. A. . .	1021	V. S. T. nucleo	Indican; phenol	Uric acid
J. B.	F	10	3/ 15 10 a. m.	L. A. . .	1024	V. S. T. nucleo	None	None
J. L.	M	6	1/19 10 a. m.	L. A. . .	1026	None	Phenol	None
J. L.	M	6	1 22 10 a. m.	L. A. . .	1020	V. S. T. nucleo	Indican; phenol	Hyaline; cylindroid
J. L.	M	6	1 24 10 a. m.	L. A. . .	1020	None	None	None
J. L.	M	6	1 25/10 a. m.	L. A. . .	1016	None	Phenol	None
R. S.	F	11	1/19/10 a. m.	L. A. . .	1017	None	None	None
R. S.	F	11	1 3 10 a. m.	L. A. . .	1020	T. nucleo	Urobilin; phenol	Calc. oxalate
R. S.	F	11	1 10 10 a. m.	L. A. . .	1018	V. S. T. nucleo	None	None
E. H.	M	6	2/ 18 10 a. m.	L. A. . .	1018	V. S. T. nucleo	None	None
E. H.	M	6	2 20 10 a. m.	L. A. . .	1020	V. S. T. nucleo	Urobilin	Calc. oxalate
E. H.	M	6	2 27 10 a. m.	L. A. . .	1018	V. S. T. nucleo	None	None
E. M.	M	6	1 30 10 a. m.	A. . . .	1020	V. S. T. nucleo	Indican	Uric acid
E. M.	M	6	1 31 10 a. m.	L. A. . .	1018	V. S. T. nucleo	None	Calc. oxalate
M. C.	F	10	2 2 10 a. m.	L. A. . .	1028	S. T. nucleo	Phenol	None
M. C.	F	10	2 22 10 a. m.	L. A. . .	1018	S. T. nucleo	None	Hyaline; cylindroid
J. C.	M	11	11/ 15, 09 a. m.	L. A. . . .	1030	S. T. nucleo;	None	Calc. oxalate
J. C.	M	11	11 18 09 a. m.	L. A. . .	1020	S. T. serum	Urobilin; phenol	None
J. C.	M	11	11 22, 09 a. m.	L. A. . .	1020	V. S. T. nucleo;	Phenol	None
J. C.	M	11	11 22, 09 a. m.	L. A. . .	1020	V. S. T. nucleo;	Phenol	None
E. C.	M	14	11 15 09 a. m.	L. A. . .	1022	S. T. nucleo	None	None
E. C.	M	14	11 22 09 a. m.	L. A. . . .	1023	V. S. T. nucleo	Phenol	None
E. C.	M	14	11 18 09 a. m.	L. A. . .	1020	V. S. T. nucleo	Urobilin; phenol	Calc. oxalate
K. K.	M	12	11 26 09 m.	L. A. . . .	1020	None	None	None
K. K.	M	12	11/27, 09 a. m.	L. A. . .	1026	V. S. T. nucleo	None	None
J. H.	F	5	11/27, 09 a. m.	L. A. . .	1017	V. S. T. nucleo	Phenol	Amorph. urates
J. H.	F	5	11/27, 09 a. m.	L. A. . .	1020	S. T. nucleo	Urobilin	None
F. K.	M	8	12 4 09 a. m.	L. A. . .	1022	V. S. T. nucleo	Phenol	None
F. K.	M	8	12 8 09 a. m.	L. A. . .	1025	V. S. T. nucleo	None	None
F. K.	M	8	12 9 09 a. m.	L. A. . . .	1020	V. S. T. nucleo	None	None
F. W.	M	2	12 22 10 a. m.	L. A. . .	1016	V. S. T. nucleo	None	None
F. W.	M	2	12 22 10 p. m.	L. A. . . .	1020	V. S. T. nucleo	None	None
J. W.	M	4	2 22 10 a. m.	L. A. . .	1016	V. S. T. nucleo	Phenol	Calc. oxalate
J. W.	M	4	2 22/10 p. m.	L. A. . .	1018	V. S. T. nucleo	Phenol	None
J. L.	M	2	11 11 09 a. m.	L. A. . . .	1016	None	Urobilin	Hyaline; cylindroid
J. L.	M	2	11 18 09 a. m.	L. A. . . .	1023	None	Phenol	None
J. L.	M	2	11 20, 09 s. m.	L. A. . .	1016	None	None	None

*No sugar, diacetic acid or acetone was found in any group. In this group, the reaction was uniformly acid.

†Here, and in the following tables, a. m. indicates morning specimens; m. noon specimens; p. m. afternoon specimens; v. specimen voided immediately after a night's rest; t. total amount of urine in twenty-four hours.

‡Here and in the succeeding tables A means amber; L. A., light amber; D. A., dark amber; P., pale.

§V. S. T. means very slight trace; S. T., slight trace; T., trace; M. T., marked trace.

specific gravity was 1,022, while in another voiding 1,250 c.c.—one of the largest amounts recorded—the specific gravity was 1,025. Neither the form nor the amount of albumin present bore any relationship whatsoever to the variations in the specific gravity or to the amounts voided.

Variations in the *reaction* had no influence on the albuminuria. In one of the cases in Group 4 (the three patients from whom samples were examined daily over a period of weeks) we noted a rather interesting condition, from which, however, no conclusions can be drawn. An evening sample of one day had a specific gravity of 1,030; it was markedly acid, contained a very slight trace of nucleo-albumin, and the sediment showed amorphous urates. The urine of the following morning showed a marked turbidity when voided, which was due to a fine white flocculent precipitate; its reaction was strongly alkaline; it contained no albumin, but showed an abundant precipitation of phosphates on boiling, and the sediment contained large quantities of earthy phosphates. A sample voided in the early afternoon of the same day, had a specific gravity of 1,028; its reaction was strongly acid and it contained a very slight trace of nucleo-albumin, the sediment showing amorphous urates and calcium oxalate crystals.

One cannot argue that the absence of albumin in the second sample was dependent on the alkaline reaction, since albumin was absent in this boy's samples not infrequently when the urine was strongly acid. But the high phosphatic content of the morning urine, wedged in between samples which were highly acid, is interesting and difficult of explanation. Its interest is greatly increased, moreover, by the fact that this is a common and not unique occurrence in the experience of this boy. On one other occasion noted in our tables, morning samples on two successive days showed in the one a highly acid urine with nucleo-albumin, and in the next a highly alkaline urine without albumin. On several occasions not recorded in our tables, we have observed this boy pass a highly alkaline urine on rising, and within a few hours void a urine which was definitely or strongly acid. We desire to emphasize the fact that the phosphates were present only in the morning samples, and, therefore, not dependent on the diet.

In none of the cases examined have we found *sugar*, *acetone*, or *diacetic acid*, and these substances may be eliminated as having any bearing on the occurrence of the type of albuminuria under discussion.

In 254 examinations, *indican* was present twenty times, *phenol* thirty-seven times, and *urobilinogen* twenty-one times. While albumin was associated with these bodies in the majority of instances, it was sometimes absent when they were all present, and the amount was never greater when associated with them than it was in the specimens in which they were absent. To state the results in fuller detail, *indican* was present

three times without albumin, and in association with phenol and without albumin five times, and once with both phenol and urobilinogen in the absence of albumin. Phenol alone was present without albumin five times.

Turning now to the possible influences of the substances demonstrable by the microscope, we would state that in no instance were *epithelial cells* or *leukocytes* present in excess of the normal. In one case, in two specimens collected on successive days, a few erythrocytes were noted, but they were not associated with casts or cylindroids. In the first of these, an evening specimen, there was present a very slight trace of nucleo-albumin, and in the second, a morning specimen, both serum and nucleo-albumin were present in very slight traces.

In considering the relationship of *crystals* to the presence of albumin, it is necessary to bear in mind the possibility that in some instances, they may have been precipitated out after the urine had been voided. This is especially likely to have occurred because we have depended entirely on low temperatures for the preservation of the specimens.

In the 248 sediment examinations, *uric acid crystals* were found alone fifty-one times. In these samples, albumin was entirely absent five times. Serum albumin was present alone in slight traces twice, and nucleo-albumin alone either in slight or very slight traces thirty-five times. In nine instances both forms were present as traces, slight traces, or very slight traces. In seven of these samples, occasional casts and cylindroids were found.

Calcium oxalate crystals were present alone in thirty-eight samples. Twelve of these had no albumin, two had serum-albumin alone in very slight traces, eighteen had nucleo-albumin alone in amounts varying from traces to very slight traces. In the six remaining cases both varieties were found in correspondingly small quantities; casts were not found in any of the samples.

Ammonium urates were present alone three times and *amorphous urates* ten times, and in twenty-two instances they were both present. The findings as to albumin were practically the same as in the case of the uric acid and calcium oxalate crystals.

In the samples containing uric acid crystals alone, casts were noted rather more often than in the samples showing the other forms of crystals, but there was no increase in the amount of albumin as compared with other specimens, nor in the amount of cellular elements. That these findings as to casts in the samples showing uric acid crystals alone is probably accidental is borne out by the fact that in thirteen samples showing both uric acid and calcium oxalate crystals occasional hyaline casts were present but once.

We do not find any evidence, therefore, to indicate that crystals, when present in amounts such as are found in the average normal child, are in

TABLE 2.—CHILDREN OF GROUP 2 FROM THE HOSPITAL WITH CONGENITAL OR ACQUIRED DEFORMITIES
(OTHER THAN TUBERCULOSIS) *

Name	Sex	Age Years	Date	Color†	Spec. Grav.	Albumin§	Indican, Urobilinogen, Phenol	Casts, Cylindroids, Crystals
H. H.	M	3	1/28/10 a. m.	L. A. . . .	1030	S. T. nucleo	None	Uric acid
H. H.	M	3	1/28/10 p. m.	L. A. . . .	1020	V. S. T. nucleo	None	None
H. H.	M	3	1/29/10 a. m.	L. A. . . .	1024	V. S. T. nucleo	None	Hyaline; cylindroid
H. H.	M	3	1/29/10 p. m.	L. A. . . .	1028	V. S. T. nucleo	None	None
F. M.	M	5	1/28/10 a. m.	A.	1022	V. S. T. serum	None	None
F. M.	M	5	1/28/10 p. m.	L. A. . . .	1030	V. S. T. nucleo	None	Calc. oxalate
F. M.	M	5	1/29/10 a. m.	L. A. . . .	1020	V. S. T. nucleo	None	Uric acid
F. M.	M	5	1/29/10 p. m.	L. A. . . .	1020	V. S. T. nucleo	None	None
F. M.	M	5	3/ 4/10 f.	D. A. . . .	1024	V. S. T. nucleo;	None	None
						V. S. T. serum		
F. M.	M	5	3/ 4/10 m.	D. A. . . .	1030	V. S. T. nucleo	None	Hyaline; cylindroid
F. M.	M	5	3/ 4/10 p. m.	A.	1027	V. S. T. nucleo	None	None
F. M.	M	5	3/ 5/10 f.	A.	1024	V. S. T. nucleo	None	None
L. B.	M	8	1/28/10 a. m.	L. A. . . .	1028	S. T. nucleo	None	Uric acid
L. B.	M	8	1/28/10 p. m.	L. A. . . .	1030	None	None	None
L. B.	M	8	1/29/10 a. m.	L. A. . . .	1024	V. S. T. nucleo	None	Not exam.
L. B.	M	8	1/31/10 a. m.	L. A. . . .	1028	None	None	None
L. B.	M	8	1/31/10 p. m.	L. A. . . .	1026	V. S. T. nucleo	None	Uric acid
L. B.	M	8	1/29/10 a. m.	L. A. . . .	1030	V. S. T. nucleo	None	Hyaline; cylindroid;
								uric acid
A. M.	M	2	1/10/10 a. m.	P.	1022	V. S. T. nucleo	Indican; phenol	Calc. oxalate
R. T.	M	4	1/11/10 a. m.	L. A. . . .	1024	V. S. T. nucleo	None	Uric acid
A. R.	F	6	1/11/10 a. m.	L. A. . . .	1025	V. S. T. serum	Indican; phenol	Uric acid
A. R.	F	6	3/31/10 f.	A.	1024	V. S. T. nucleo;	Not exam.	Not exam.
						V. S. T. serum		
A. R.	F	6	3/31/10 p. m.	L. A. . . .	1020	V. S. T. nucleo;	Not exam.	Hyaline; cylindroid
						V. S. T. serum		
R. P.	M	3	3/31/10 f.	L. A. . . .	1024	None	None	Calc. oxalate
L. K.	F	8	3/31/10 f.	L. A. . . .	1024	V. S. T. nucleo	Indican	None
F. B.	F	9	3/31/10 f.	L. A. . . .	1014	V. S. T. nucleo	None	Calc. oxalate
S. H.	F	2	3/31/10 f.	L. A. . . .	1030	V. S. T. nucleo	None	None
C. S.	F	8	3/31/10 f.	L. A. . . .	1016	V. S. T. nucleo	Indican	Not exam.
C. S.	F	8	3/31/10 p. m.	L. A. . . .	1020	V. S. T. nucleo	Indican	Hyaline; cylindroid
F. S.	M	10	3/31/10 f.	L. A. . . .	1018	V. S. T. nucleo	Not exam.	Uric acid
F. S.	M	10	3/31/10 p. m.	L. A. . . .	1020	V. S. T. nucleo	None	None
K. L.	M	5 1/2	3/30/10 p. m.	A.	1028	None	None	Cylindroid
K. L.	M	5 1/2	3/31/10 f.	A.	1028	V. S. T. nucleo;	None	Uric acid
						V. S. T. serum	None	Cylindroid
F. W.	M	3	3/29/10 p. m.	D. A. . . .	1036	V. S. T. nucleo	None	Occas. R. B. C.
F. W.	M	3	3/30/10 f.	D. A. . . .	1030	V. S. T. nucleo;	None	Occas. R. B. C.;
						V. S. T. serum		Calc. oxalate

K. D.	F	7	3/29/10 p. m.	D. A...	1030	V. S. T. nucleo	None	None
K. D.	F	7	3/30/10 r. m.	D. A...	1028	V. S. T. nucleo	Urobilin	None
M. H.	F	7	3/29/10 p. m.	D. A...	1032	V. S. T. nucleo	None	None
M. H.	F	7	3/30/10 r. m.	D. A...	1032	V. S. T. nucleo	None	Not exam.
J. C.	M	3	3/29/10 r. m.	L. A...	1032	V. S. T. nucleo	None	None
J. C.	M	3	3/29/10 a. m.	L. A...	1026	V. S. T. nucleo;	Hyaline ; cylindroid	None
						V. S. T. serum		
M. C.	M	10	12/ 9/09 a. m.	L. A...	1020	V. S. T. nucleo	None	None
H. A.	M	3	12/ 9/09 a. m.	L. A...	1027	S. T. nucleo	Hyaline ; cylindroid	None
A. M.	M	6	12/ 9/09 a. m.	L. A...	1010	None	None	None
M. O.	M	4	12/ 9/09 a. m.	L. A...	1014	V. S. T. nucleo	None	None
W. J.	M	8	12/ 9/09 a. m.	L. A...	1016	V. S. T. serum	None	None
R.	F	10	12/10/09 a. m.	L. A...	1027	V. S. T. nucleo ;	Calc. oxalate	None
						S. T. serum		
F. B.	F	5	12/10/10 a. m.	L. A...	1024	S. T. serum	None	None
H. D.	M	5	12/15/09 a. m.	D. A...	1020	None	Calc. oxalate	None
H. C.	M	5	12/15/09 a. m.	L. A...	1025	None	Calc. oxalate	None
E. C.	M	7	12/ 9/09 a. m.	L. A...	1022	None	Amorph. urates ;	None
							calc. oxalate	
B. B.	M	8	12/10/09 a. m.	L. A...	1026	None	None	None
D. B.	F	2	11/11/09 a. m.	L. A...	1020	V. S. T. nucleo	Phenol	None
D. B.	F	2	12/12/09 a. m.	L. A...	1018	V. S. T. nucleo	None	None
M. C.	M	11	1/28/10 p. m.	L. A...	1022	None	None	None
M. C.	M	11	1/29/10 a. m.	L. A...	1024	None	None	Not exam.
M. C.	M	11	2/24/10 p. m.	P.	1020	None	Uric acid	None
M. C.	M	11	2/25/10 r. m.	L. A...	1020	None	None	None
M. C.	M	11	2/25/10 a. m.	L. A...	1027	V. S. T. nucleo ;	Hyaline ; cylindroid	None
M. C.	M	11	2/25/10 a. m.	L. A...	1030	S. T. nucleo ;	Ammon. urates	None
						S. T. serum	Ammon. urates	
M. C.	M	11	2/25/10 p. m.	L. A...	1014	V. S. T. nucleo	None	None
M. C.	M	11	2/26/10 r. m.	L. A...	1014	V. S. T. nucleo	Uric acid	None
M. C.	M	11	2/26/10 a. m.	L. A...	1020	S. T. nucleo	Hyaline ; cylindroid	None
M. C.	M	11	2/26/10 m.	L. A...	1020	S. T. nucleo	Uric acid	None
M. C.	M	11	2/26/10 p. m.	L. A...	1025	V. S. T. nucleo	Uric acid	None
M. C.	M	11	2/27/10 r. m.	L. A...	1012	V. S. T. nucleo	None	None
M. C.	M	11	2/27/10 a. m.	L. A...	1014	None	None	None
M. C.	M	11	2/27/10 p. m.	L. A...	1020	V. S. T. nucleo	None	None
M. C.	M	11	2/28/10 r. m.	L. A...	1025	V. S. T. nucleo	None	None
M. C.	M	11	2/28/10 a. m.	L. A...	1026	S. T. nucleo	Not exam.	None
M. C.	M	11	2/28/10 m.	L. A...	1025	S. T. nucleo	None	None
M. C.	M	11	2/28/10 p. m.	L. A...	1012	None	None	None
M. C.	M	11	3/ 1/10 r. m.	L. A...	1012	V. S. T. nucleo	Not exam.	None
M. C.	M	11	3/ 1/10 a. m.	L. A...	1014	None	None	None
M. C.	M	11	3/ 1/10 m.	L. A...	1020	None	Not exam.	None
M. C.	M	11	3/ 1/10 p. m.	L. A...	1018	V. S. T. nucleo	Not exam.	None

*The reaction was uniformly acid. Significance of abbreviations same as in previous table.

any way responsible for the associated albumin. In the children in Group 4, whose urines were examined over a period of weeks, we have several times found uric acid crystals present without albumin. The same can be said of the various other crystals, and it is also true that the amounts of albumin varied in the same way when associated with crystals as when present without them.

The *stools* were examined seventy times in sixty-nine different children. In fifty children they were normal, in the nineteen remaining there were moderate variations from the normal; such as offensive odor, abnormal consistence, undigested food particles, starch granules and fat. The results of the examinations for albumin in the urines of these two groups showed absolutely no difference as to the frequency of occurrence, the quantity eliminated, or the form of the albumin. Thus, in one instance in the latter group albumin was absent when the stool was unformed, malodorous, soft and mushy, with slight fermentation, and showing starch granules microscopically. Therefore, we conclude that these mild disturbances of the intestinal digestion in apparently normal children, discoverable only by examination of the stools, are not sufficient to account for the occurrence of the albumin. This conclusion is fully confirmed by our findings in severe cases of intestinal indigestion, which sometimes show no albumin and rarely give more marked reactions for albumin than those we have noted in these presumably normal children.

Complete physical examinations were made in all the cases except those comprising Group 2. In these, evidences of disease were eliminated by the hospital records. In our own examinations we gave special attention to the cardiovascular system, in order to eliminate valvular and myocardial changes, degenerations of the vessels, and variations in the arterial tension. We found murmurs of a functional nature very common, but in no way related to the presence of albumin. All cases with evidences of organic disease, of which we met several in the course of our studies, were excluded. In Group 3, we made systematic studies of the blood-pressure in both the upright and recumbent postures. The systolic pressure varied in these thirty-six cases from eighty-five to 119, the average being about 100. The differences in pressure between the upright and the recumbent was insignificant, about 5 mm. on the average. The figures 85 to 119 are probably within the normal range of variation, if one considers the nervous influences which were active in consequence of the examinations. In some children the effect of these influences was to increase the arterial tension, while in others, the pressure was lowered. In several instances the pressure, which was primarily low or high, rapidly returned to the normal after the child had become accustomed to the examination. In any event, the urinary findings as to albumin were

the same in high and low pressures and in neither were they different from the findings in those cases with blood-pressures at or near 100.

The great majority of the children whose urines we have studied have been on mixed and varied diets. In three instances, however, in which we were able to control the children, we have studied the urine while they were on their ordinary diets, and again while they were on exclusive milk diets.

In the first case two examinations were made at intervals of two days while the child was on a mixed diet. In the first sample examined there was present a trace of both serum and nucleo-albumin, and in the second a very slight trace of nucleo-albumin. After the child had been on an exclusive milk diet for one week, another specimen was examined, which contained a trace of both serum and nucleo-albumin. An examination made two days later showed slight traces of each.

In the second case an examination made while the child was on a mixed diet showed a very slight trace of nucleo-albumin. A second examination, made after the child had been on an exclusive milk diet for two days, gave the same result, as did also the third examination, which was made after the milk diet had been continued for twelve days.

The third case is the one previously referred to under Group 2, in which the urine was examined for six successive days. On the first day while the child was on a mixed diet, one examination was made which showed no albumin. On the second day four specimens were examined; the first showed no albumin; the second a very slight trace of nucleo-albumin; the third a slight trace of both albumins, and the fourth a very slight trace of nucleo-albumin.

On the third day, while the child was still on a mixed diet, four examinations were made. The first showed a very slight trace of nucleo-albumin; the second and third slight traces of nucleo-albumin, and the fourth a very slight trace of serum-albumin.

On the fourth day, the mixed diet being continued, the results of three examinations showed in the first a very slight trace of nucleo-albumin; in the second no albumin, and in the third a very slight trace of nucleo-albumin.

On the fifth day, while the child was on a milk diet, four examinations showed in the first a very slight trace of nucleo-albumin; in the second and third slight traces, and in the fourth no albumin.

On the sixth day, the milk diet being continued, the first of three examinations showed a very slight trace of nucleo-albumin and the others no albumin.

These few results are of course in no sense conclusive, but in so far as they go, they suggest that there is no difference in the albumin elimination of the two kinds of diet described. One might infer that in Case 3 the results did indicate a difference, were it not that this same child on

TABLE 3.—CHILDREN FROM THE BAPTIST ORPHANAGE OF PHILADELPHIA (GROUP 3) *

Name	Age	Date	Total Amt. c. c.	Color	Spec. Grav.	Albumin§	Indican, Uro- bilinogen, Phenol	Cast, Cylindroids, Crystals
W. K.	11	3/25/10 t.	1020	L. A.	1024	V. S. T. nucleo	None	None
.....	..	3/25/10 a. m.		L. A.	1010	V. S. T. nucleo		Uric acid
.....	..	3/25/10 m.		L. A.	1022	None		Uric acid
.....	..	3/25/10 p. m.		P. A.	1012	None		None
.....	..	3/26/10 r.		A.	1026	None		Not exam.
C. B.	11	3/25/10 t.	700	L. A.	1020	V. S. T. nucleo; V. S. T. serum	None	Cylindroid
.....	..	3/25/10 a. m.		L. A.	1028	S. T. serum		
.....	..	3/25/10 m.		A.	1030	S. T. nucleo; S. T. serum		
.....	..	3/25/10 p. m.		L. A.	1020	S. T. nucleo		
.....	..	3/26/10 r.		L. A.	1022	V. S. T. nucleo		
A. S.	11	3/20/10 t.	650	L. A.	1020	V. S. T. nucleo	None	Uric acid
.....	..	3/20/10 a. m.		L. A.	1024	None		
.....	..	3/20/10 m.		P.	1016	S. T. serum		
.....	..	3/20/10 p. m.		P.	1020	None		
.....	..	3/21/10 r.		L. A.	1030	None		
W. A.	5	3/27/10 t.	575	L. A.	1017	V. S. T. nucleo	Indican	Uric acid
.....	..	3/27/10 a. m.		P.		V. S. T. nucleo		
.....	..	3/27/10 m.		P.		V. S. T. nucleo		
.....	..	3/27/10 p. m.		L. A.	1026	V. S. T. nucleo		
.....	..	3/28/10 r.		P.	1012	V. S. T. nucleo		
N. W.	4	3/15/10 t.	600	L. A.	1025	V. S. T. nucleo; V. S. T. serum	None	None
.....	..	3/15/10 a. m.		P.	1028	V. S. T. nucleo		
.....	..	3/15/10 m.		P.	1020	V. S. T. nucleo		
.....	..	3/15/10 p. m.		P.	1022	S. T. nucleo		
.....	..	3/16/10 r.		D. A.	1032	S. T. nucleo; V. S. T. serum		
C. S.	12	3/28/10 t.	625	A.	1032			
.....	..	3/28/10 a. m.		A.	1030	None		
.....	..	3/28/10 p. m.		A.		V. S. T. nucleo		
C. W.	7	3/16/10 t.	550	L. A.	1028	V. S. T. nucleo; V. S. T. serum	None	Hyaline; cylindroid
.....	..	3/16/10 m. ⁶⁻²		L. A.	1025	V. S. T. nucleo; S. T. serum		
.....	..	3/16/10 p. m.		L. A.	1026	V. S. T. nucleo; V. S. T. serum		

.....	..	3/17/10 r.		A.	1028	V. S. T. nucleo; V. S. T. serum		
E. C.	6	3/17/10 t.	625	L. A.	1022	V. S. T. nucleo	Phenol	Uric acid
.....	..	3/17/10 m.		P.	1025	V. S. T. nucleo		
.....	..	3/17/10 p.		P.	1025	V. S. T. nucleo		
.....	5	3/17/10 r.	525	D. A.	1030	V. S. T. nucleo		
.....	..	3/18/10 t.		L. A.	1030	V. S. T. nucleo	Urobilin	Uric acid
.....	..	3/18/10 a.		A.	1029	V. S. T. nucleo		
.....	..	3/18/10 m.		A.	1028	V. S. T. nucleo		
.....	..	3/19/10 p.		D. A.	1030	V. S. T. nucleo		
J. S.	6	3/15/10 t.	450	P.	1023	V. S. T. serum	None	None
.....	..	3/15/10 a.		P.	1020	V. S. T. serum		
.....	..	3/15/10 m.		P.	1025	V. S. T. serum		
.....	..	3/16/10 p.		D. A.		V. S. T. serum		
P. K.	6	3/17/10 t.	300	A.	1030	V. S. T. nucleo; V. S. T. serum	None	Hyaline; cylindroid; uric acid
.....	..	3/16/10 m.		A.	1030	None		
.....	..	3/16/10 p.		A.	1030	V. S. T. nucleo		
.....	..	3/17/10 r.		A.	1028	V. S. T. nucleo		
E. W.	5	3/17/10 t.	670	P.	1025	V. S. T. nucleo	None	Hyaline; cylindroid; uric acid
.....	..	3/17/10 a.		P.	1022	V. S. T. nucleo		
.....	..	3/17/10 m.		P.	1024	S. T. nucleo		
.....	..	3/17/10 p.		P.	1025	V. S. T. nucleo		
.....	..	3/18/10 r.		L. A.	1030	V. S. T. nucleo		
E. C.	7	3/15/10 t.	515	L. A.	1025	V. S. T. nucleo; V. S. T. serum	None	None
.....	..	3/15/10 a.		L. A.	1025	V. S. T. serum		
.....	..	3/15/10 m.		L. A.	1028	None		
.....	..	3/15/10 p.		A.	1028	V. S. T. nucleo; V. S. T. serum		
.....	..	3/16/10 r.		D. A.	1035	V. S. T. nucleo; V. S. T. serum		
F. S.	12	3/21/10 t.	775	L. A.	1022	V. S. T. nucleo	None	Hyaline; cylindroid; uric acid
.....	..	3/21/10 a.		L. A.	1020	V. S. T. nucleo		
.....	..	3/21/10 m.		P.	1012	S. T. nucleo		
.....	..	3/21/10 p.		L. A.	1024	V. S. T. nucleo		
.....	..	3/22/10 r.		D. A.	1022	V. S. T. nucleo		
J. K.	13	3/21/10 t.	1250	L. A.	1025	V. S. T. nucleo	None	Hyaline; cylindroid; calc. oxalate
.....	..	3/21/10 a.				V. S. T. nucleo		

TABLE 3.—(CONTINUED)

Name	Age	Date	Total Amt. c.c.	Color	Spec. Grav.	Albumin	Indican, Uro- bilinogen, Phenol	Casts, Cylindroids, Crystals
.....	..	3/21/10 m.	...			V. S. T. nucleo		
.....	..	3/21/10 p. m.				V. S. T. nucleo		
.....	..	3/22/10 f.				V. S. T. nucleo		
J. F.	11	3/22/10 f.	600	L. A.	1020	V. S. T. nucleo	None	None
.....	..	3/22/10 a. m.		L. A.	1030	V. S. T. nucleo		
.....	..	3/22/10 m.		F.	1018	V. S. T. nucleo; V. S. T.		
.....	11	3/22/10 p. m.		L. A.	1025	serum		
.....	..	3/23/10 f.		D. A.	1025	serum		
E. A.	11	3/22/10 t.	1020	L. A.	1020	V. S. T. nucleo	None	None
.....	..	3/22/10 a. m.				V. S. T. nucleo; V. S. T.	None	None
.....	..	3/22/10 m.				serum	None	None
.....	..	3/22/10 p. m.				V. S. T. nucleo	None	None
.....	..	3/23/10 f.				V. S. T. nucleo	None	None
J. H. B.	8	3/26/10 f.	500	A.	1030	V. S. T. nucleo	Phenol	Amorph. urates
.....	..	3/26/10 a. m.		A.	1030	None		
.....	..	3/26/10 m.			1027	None		
.....	..	3/26/10 p. m.			1027	None		
.....	..	3/27/10 f.			1032	V. S. T. nucleo		
R. D.	10	3/26/10 t.	650	L. A.	1020	V. S. T. nucleo	Phenol	Hyaline; cylindroid; uric acid
.....	..	3/26/10 a. m.		L. A.	1024	V. S. T. nucleo		
.....	..	3/26/10 m.		L. A.	1026	V. S. T. nucleo		
.....	..	3/26/10 p. m.		A.	1022	S. T. nucleo; V. S. T.		
.....	..	3/27/10 f.		A.	1022	serum		
.....	..	3/27/10 r.		A.	1022	V. S. T. nucleo; V. S. T.		
R. T.	8	3/26/10 t.	500	L. A.	1026	serum		
.....	..	3/26/10 a. m.		L. A.	1026	V. S. T. nucleo	None	Amorph. urates
.....	..	3/26/10 m.		L. A.	1032	V. S. nucleo		
.....	..	3/26/10 p. m.		A.	1032	None		
.....	..	3/27/10 f.		A.		S. T. nucleo		
.....	..	3/27/10 p.		A.		V. S. T. nucleo		
E. L.	9	3/26/10 t.	600	A.	1028	V. S. T. nucleo	None	Amorph. urates; uric acid
.....	..	3/18/10 a. m.		A.	1028	V. S. T. nucleo		
.....	..	3/18/10 m.		L. A.	1025	V. S. T. nucleo		
.....	..	3/18/10 p. m.		A.	1028	V. S. T. nucleo		

.....	..	3/19/10 r.		A.	1028	V. S. T. nucleo		
D. F.	9	3/19/10 t.	975	P.	1025	V. S. T. nucleo; V. S. T. serum	None	Hyaline; cylindroid
.....	..	3/19/10 a. m.		P.	1022	V. S. T. nucleo		
.....	..	3/19/10 m.		P.	1020	None		
.....	..	3/19/10 p. m.		A.	1022	V. S. T. nucleo; S. T. serum		
.....	..	3/19/10 r.		A.	1030	V. S. T. nucleo; V. S. T. serum		
E. A.	7	3/16/10 t.	560	A.	1030	V. S. T. nucleo; V. S. T. serum	None	Uric acid
.....	..	3/16/10 m.		A.	1028	V. S. T. nucleo		
.....	..	3/16/10 p. m.		A.	1030	V. S. T. nucleo		
.....	..	3/16/10 r.		A.	1032	V. S. T. nucleo		
J. C.	9	3/19/10 t.	700	L. A.	1020	V. S. T. nucleo; V. S. T. serum	None	Not exam.
.....	..	3/19/10 a. m.		L. A.	1022	V. S. T. nucleo; V. S. T. serum		
.....	..	3/19/10 m.		P.	1020	V. S. T. nucleo		
.....	..	3/19/10 p. m.		P.	1012	V. S. T. nucleo		
.....	..	3/20/10 r.		L. A.	1025	V. S. T. nucleo; V. S. T. serum		
F. B.	7	3/19/10 t.	775	L. A.	1020	V. S. T. nucleo; V. S. T. serum	None	Not exam.
.....	..	3/19/10 a. m.		L. A.	1020	V. S. T. nucleo		
.....	..	3/19/10 p. m.		P.	1022	None		
.....	..	3/20/10 r.		L. A.	1025	S. T. nucleo		
.....	..	3/20/10 t.		L. A.	1028	V. S. T. nucleo		
M. A.	8	3/27/10 t.	775	L. A.	1016	V. S. T. nucleo	None	Hyaline; uric acid
.....	..	3/27/10 a. m.		L. A.	1024	V. S. T. nucleo		
.....	..	3/27/10 m.		L. A.	1012	V. S. T. nucleo		
.....	..	3/27/10 p. m.		L. A.	1014	V. S. T. nucleo		
.....	..	3/28/10 r.		A.	1018	V. S. T. nucleo		
A. P.	10	3/27/10 t.	575	L. A.	1027	V. S. T. nucleo	None	Calc. oxalates
.....	..	3/27/10 a. m.		L. A.	1026	None		
.....	..	3/27/10 m.		L. A.	1025	None		
.....	..	3/27/10 p. m.		A.	1028	V. S. T. nucleo		
.....	..	3/28/10 r.		L. A.	1025	V. S. T. nucleo		
J. B.	10	3/20/10 t.	775	L. A.	1020	V. S. T. nucleo; V. S. T. serum	Phenol	None
.....	..	3/20/10 a. m.		L. A.	1022	S. T. nucleo; S. T. serum		
.....	..	3/20/10 m.		L. A.	1018	S. T. nucleo; V. S. T. serum		

TABLE 3.—(CONTINUED)

Name	Age	Date	Total Amt. c.c.	Color	Spec. Grav.	Albumin§	Indican, Uro- bilinogen, Phenol	Casts, Cyli- ndroids, Crystals
.....	..	3/20/10 p. m.		A.	1026	S. T. nucleo; V. S. T. serum		
.....	..	3/20/10 r.		L. A.	1018	V. S. T. nucleo		
†	..			A.	1024	None		
†	..			L. A.	1026	None		
V. D.	7	3/18/10 t.	700	L. A.	1025	T. nucleo; S. T. serum	None	Hyaline; cylindroid; uric acid
.....	..	3/18/10 a. m.		P.	1025	V. S. T. nucleo; S. T. serum		
.....	..	3/18/10 m.		P.	1025	T. nucleo; S. T. serum		None
.....	..	3/18/10 p. m.		A.	1030	M. T. nucleo; M. T. serum		None
.....	..	3/19/10 r.		A.	1030	V. S. T. nucleo		
.....	..	3/21/10 t.	600	L. A.	1018	T. nucleo; T. serum		Hyaline; cylindroid; uric acid; calc. oxal- ate
.....	..	3/21/10 a. m.		A.	1030	T. serum; T. nucleo		None
.....	..	3/21/10 m.		L. A.	1020	T. nucleo; T. serum		None
.....	..	3/21/10 p. m.		A.	1030	M. T. nucleo; M. T. serum		None
.....	..	3/22/10 r.		A.	1030	S. T. nucleo; S. T. serum		
†	..			P.	1022	V. S. T. nucleo; V. S. T. serum		
†	..			P.	1022	V. S. T. nucleo; V. S. T. serum		
.....	..	3/21/10 r.		A.	1030	V. S. T. nucleo		
II. M.	12	3/22/10 t.	600	L. A.	1024	S. T. nucleo; S. T. serum	Phenol	None
.....	..	3/22/10 a. m.		L. A.	1014	None		
.....	..	3/22/10 m.		L. A.	1020	T. nucleo; M. T. nucleo		
.....	..	3/22/10 p. m.		L. A.	1030	V. S. T. nucleo; V. S. T. serum		
.....	..	3/23/10 r.		D. A.	1026	S. T. nucleo		
†	..			L. A.	1026	S. T. nucleo; S. T. serum		
†	..			L. A.	1026	S. T. nucleo; S. T. serum		
E. S.	3	3/24/10 t.	550	L. A.	1022	V. S. T. nucleo	None	None

.....	..	3/24/10 a. m.		L. A.	1022	None		
.....	..	3/24/10 m.		P. A.	1008	None		
.....	..	3/24/10 p. m.		L. A.	1025	None		
.....	..	3/25/10 r.		L. A.	1025	V. S. T. nucleo		
F. M.	8	3/24/10 t.	550	L. A.	1024	V. S. T. nucleo	None	None
.....	..	3/24/10 a. m.		L. A.	1023	V. S. T. nucleo		
.....	..	3/24/10 m.		L. A.	1026	S. T. nucle		
.....	..	3/24/10 p. m.		A.	1032	S. T. nucle		
.....	..	3/25/10 r.		A.	1030	V. S. T. nucle		
H. W.	12	3/24/10 t.	1000	L. A.	1020	V. S. T. nucle	None	None
.....	..	3/24/10 a. m.		L. A.	1022	None		
.....	..	3/24/10 m.		P. A.	1008	None		
.....	..	3/24/10 p. m.		L. A.	1025	None		
.....	..	3/25/10 r.		L. A.	1025	V. S. T. nucle		
R. H.	12	3/23/10 t.	700	L. A.	1024	V. S. T. nucle	None	None
.....	..	3/23/10 a. m.		L. A.	1024	V. S. T. nucle		
.....	..	3/23/10 m.		L. A.	1024	V. S. T. nucle		
.....	..	3/23/10 p. m.		A.	1030	None		
.....	..	3/24/10 r.		A.	1032	None		
C. B.	7	3/28/10 t.	475	L. A.	1022	S. T. nucle; V. S. T. serum	None	Amorph. urates
.....	..	3/28/10 a. m.		L. A.	1022	M. T. nucle; S. T. serum		
.....	..	3/28/10 m.		L. A.	1022	S. T. nucle; S. T. serum		
C. B.	..	3/28/10 p. m.		L. A.	1020	S. T. nucle; V. S. T. serum		
.....	..	3/28/10 r.		A.	1030	S. T. nucle; V. S. T. serum		
R. M.	9	3/28/10 t.	500	L. A.	1022	None	None	None
.....	..	3/28/10 a. m.		L. A.	1030	V. S. T. nucle		
.....	..	3/28/10 m.		L. A.	1022	V. S. T. nucle		
.....	..	3/28/10 p. m.		L. A.	1022	V. S. T. nucle		
.....	..	3/29/10 r.		L. A.	1020	V. S. T. nucle		

*Reaction acid throughout. Abbreviations as in previous tables.

†Recurrent.

‡Upright.

several previous occasions had shown no albumin in his urine when on a mixed diet. This case, however, illustrates well a common characteristic of these albuminurias, which it may be well to emphasize here, and that is their marked variability. Different samples on the same day showed sometimes no albumin, and again nucleo-albumin, and at other times first nucleo-albumin and later serum-albumin.

Throughout our studies, we have borne in mind the *relationship of posture to the elimination of albumin*. In no instance have we obtained evidence which we consider sufficient to justify us in classifying any of our cases under the heading of postural or orthostatic albuminuria. In forty-nine children, however, we have endeavored to exclude the factor of position by having them void urine immediately on waking. Thirty-six of these (Group 3) were studied successively in groups of three. These children slept in a room with a trained nurse. No mechanical means were used to restrain them, but they were under the close supervision of a conscientious and interested observer, and in so far as she could determine, they neither sat up in bed nor were out of bed during the night. At 6 a. m. they were wakened and required to void urine immediately. The remaining thirteen (Group 2) were treated in the same manner by the night nurse on duty, but as her requirements occasionally took her from the ward, it is reasonable to assume that they were less well controlled.

In two children in the group of thirty-six, we considered the possibility of this relationship mainly because of the amount of albumin sometimes noted, which at its highest was recorded as a marked trace of both serum and nucleo-albumin. For this reason, in addition to the specimen voided on rising, we studied two samples voided after periods of rest during the day. The bladders were emptied and the children at once placed in the recumbent posture where they were kept until they desired to void urine again. On one occasion, the specimens voided after the night's rest as well as those voided after the day's rest showed less albumin than at some other hours of the day, but it was, nevertheless, present. The morning urine in one showed only slight and in the other very slight traces of nucleo-albumin. On the other hand, one of these boys voided a sample at 9 a. m. which contained no albumin, and neither of them showed a decrease in the amount of albumin at the end of the day, one of them in fact showing marked traces in the evening. Throughout the day, the amounts varied markedly. In other words, in neither of these cases did the findings correspond to the accepted requirements for this form of albuminuria.

Owing to the fact that albumin was occasionally present in marked traces in these two cases and because one of them showed a very few casts and cylindroids, it would seem almost more difficult to eliminate the possibility of nephritis than to eliminate the orthostatic form of albuminuria. As against this view, we would point out that in one of these cases, albu-

min was absent on one occasion, and in both, the amount of albumin fluctuated from hour to hour, varying from a very slight to a marked trace. Furthermore, there was nothing in the condition of the children to suggest a lesion of the kidneys. Both were unusually well nourished; their color was good; they had no symptoms of ill health; and their cardiovascular conditions showed nothing abnormal.

The study of the *presence of casts and cylindroids* in these groups of cases shows that twenty-eight children, or 22.5 per cent., had occasional hyaline casts associated with cylindroids, and six had cylindroids without casts. In some of them, more than one specimen showed these formed elements. Taking the total number of specimens (amounting to forty) we find that casts and cylindroids were associated thirty-three times and cylindroids were present alone seven times. The relationship of these formed elements to albumin was as follows: Of the thirty-three specimens showing both casts and cylindroids, one showed no albumin, twenty-six very slight traces of nucleo-albumin, two a slight trace, one a trace, two others a very slight trace of serum-albumin, and one a very slight trace of both serum and nucleo-albumin. Of the seven specimens showing cylindroids alone, two showed no albumin, three a very slight trace of nucleo-albumin, and two very slight traces of both serum and nucleo-albumin.

Many of the older writers contend that the occurrence of casts and cylindroids in the urine is an indication of a permanent impairment of renal function. The views of recent writers, however, have been more liberal. Jehle makes the statement that "the occurrence of casts, erythrocytes, and various epithelial cells is not necessarily a criterion of nephritis, since they are found in the urine of lordotics." Fischl supports this view and is especially impressed by it, since it fully confirms results which he obtained in animal experimentation; by suspending rabbits as well as by producing in them an artificial lordosis, he was able to demonstrate the above-mentioned elements in the urine. One of the animals which he killed showed no microscopic changes in the kidneys other than congestion, and three of the others in this series, after being released for a period of time, voided entirely normal urine.

We are inclined to believe that these elements as we have found them are merely products of a temporarily overtaxed kidney, resulting from variations in the habits of life of the individual which are so slight as to be difficult of recognition.

We now come to a consideration of the *albumins*. In the urines of 124 children we found albumin at some time in 110, or in 88.7 per cent. Albumin was present in two forms: (1) serum-albumin, and (2) an albuminous body which was precipitated by acetic acid in the cold. For purposes of convenience, but with a full appreciation of the unsettled

TABLE 4.—THREE CHILDREN (GROUP 4) WHOSE URINES WERE EXAMINED
PRACTICALLY EVERY DAY FOR SEVERAL WEEKS

Name	Age Yrs.	Am't c. c.	Date	Color	Reaction*	Spec. Grav.	Albumin	Indican, Urobil- inogen, Phenol	Casts, Cylindroids, Crystals
II. II.	8		11/ 1/09 a. m.	P.	+	1024	V. S. T. serum	None	None
.....	..		11/ 2/09 a. m.	P.	+	1022	V. S. T. serum	None	Calc. oxalate
.....	..		11/ 3/09 a. m.	L. A.	+	1024	V. S. T. serum	None	Uric acid; calc. oxalate
.....	..		11/ 4/09 a. m.	L. A.	+	1026	V. S. T. nucleo; V. S. T.	None	None
.....	..		11/ 5/09 a. m.	L. A.	+	1020	V. S. T. nucleo; V. S. T.	None	None
.....	..		11/ 6/09 a. m.	L. A.	+	1022	V. S. T. nucleo	None	Uric acid; calc. oxalate
.....	..		11/ 7/09 p. m.	D. A.	+	1023	S. T. nucleo	Phenol	Hyaline; cylindroids; uric acid
.....	..		11/ 8/09 a. m.	L. A.	+	1023	None	None	None
.....	..		11/ 9/09 a. m.	L. A.	+	1023	V. S. T. nucleo	None	None
.....	..		11/10/09 a. m.	L. A.	+	1020	V. S. T. nucleo; V. S. T.	None	None
II. II.	..	950	11/12/09 a. m.	L. A.	+	1026	V. S. T. nucleo	None	None
.....	..	950	11/15/09 t.	L. A.	+	10233	V. S. T. nucleo; V. S. T.	None	None
.....	..		11/15/09 p. m.	L. A.	+	10230	None	None	None
.....	..		11/17/09 p. m.	L. A.	+	1030	S. T. nucleo	None	None
.....	..		11/17/09 a. m.	P.	+	1028	S. T. nucleo	None	None
.....	..		11/18/09 a. m.	D. A.	+	1027	S. T. serum	None	Calc. oxalate
.....	..		11/18/09 p. m.	L. A.	+	1025	T. nucleo	None	Uric acid
.....	..		11/19/09 a. m.	L. A.	+	1022	T. nucleo	None	Uric acid; calc. oxalate
.....	..		11/20/09 a. m.	L. A.	+	1025	S. T. nucleo; S. T.	None	None
.....	..	1050	11/22/09 t.	D. A.	+	1020	V. S. T. nucleo	None	Calc. oxalate
.....	..		11/23/09 a. m.	L. A.	+	1026	V. S. T. nucleo	None	None
.....	..		11/24/09 a. m.	L. A.	+	1022	S. T. nucleo	Not exam.	Amorph. urates
.....	..		11/26/09 m.	P.	+	1022	S. T. nucleo; S. T.	None	None
.....	..		11/27/09 a. m.	L. A.	+	1020	S. T. nucleo	None	Calc. oxalates
.....	..		11/27/09 p. m.	L. A.	+	1024	S. T. nucleo	None	Amorph. urates
.....	..		12/ 2/09 m.	L. A.	+	1022	V. S. T. nucleo	None	Uric acid
II. II.	10		12/ 3/09 m.	P.	+	1020	V. S. T. nucleo	None	None
.....	..		12/ 4/09 a. m.	L. A.	+	1020	V. S. T. nucleo	None	Calc. oxalate
.....	..		12/ 5/09 m.	L. A.	+	1022	V. S. T. nucleo	None	None
.....	..		12/ 6/09 a. m.	L. A.	+	1024	V. S. T. nucleo	None	None
McC. H.	10		11/ 1/09 a. m.	L. A.	+	1020	None	None	None
.....	..		11/ 2/09 a. m.	D. A.	+	1028	V. S. T. nucleo; V. S. T.	None	None
.....	..		11/ 3/09 a. m.	L. A.	+	1028	None	None	Amorph. urates
.....	..		11/ 4/09 a. m.	L. A.	+	1026	V. S. T. nucleo; V. S. T.	Indican	Uric acid

.....	..		11/ 5/09 a. m.	L. A.	+	1026	V. S. T. nucleo	None	None
.....	..		11/ 6/09 a. m.	L. A.	+	1024	None	None	None
.....	..		11/ 7/09 p. m.	D. A.	+	1021	None	None	Uric acid; amorph. urates
.....	..		11/ 8/09 a. m.	L. A.	+	1021	V. S. T. nucleo; V. S. T.	None	Uric acid; calc. oxalate
.....	..		11/ 9/09 m.	L. A.	+	1024	S. T. nucleo	None	Calc. oxalate
.....	..		11/10/09 a. m.	D. A.	+	1022	S. T. nucleo	None	Hyaline; cylindroid; uric acid; calc. oxalate
.....	..		11/12/09 a. m.	L. A.	+	1023	V. S. T. nucleo; V. S. T. serum	None	Calc. oxalate
MeC. II.	..	975	11/15/09 t.	L. A.	+	1020	None	None	None
.....	..		11/17/09 p. m.	L. A.	+	1020	None	None	Calc. oxalate
.....	..		11/17/09 a. m.	L. A.	+	1022	V. S. T. nucleo	None	Uric acid
.....	..		11/18/09 a. m.	L. A.	+	1020	V. S. T. nucleo; V. S. T. serum	None	Calc. oxalate
.....	..		11/18/09 p. m.	L. A.	+	1018	V. S. T. nucleo; V. S. T. serum	None	Cylindroid; uric acid; ammon. urates
.....	..		11/19/09 a. m.	D. A.	+	1027	V. S. T. nucleo; V. S. T. serum	None	Uric acid
.....	..		11/20/09 a. m.	L. A.	+	1024	V. S. T. nucleo	None	None
.....	..	975	11/22/09 t.	L. A.	+	1022	V. S. T. nucleo; V. S. T. serum	None	Uric acid
.....	..		11/23/09 a. m.	L. A.	+	1027	V. S. T. nucleo	None	Amorph. urates; calc. oxalate
.....	..		11/24/09 a. m.	L. A.	+	1024	None	Not exam.	None
.....	..		11/27/09 a. m.	L. A.	+	1024	S. T. nucleo	None	None
.....	..		12/ 2/09 m.	L. A.	+	1022	None	None	Amorph. urates
.....	..		12/ 2/09 p. m.	L. A.	+	1021	None	None	Not exam.
.....	..		12/ 4/09 a. m.	L. A.	+	1024	S. T. serum	Not exam.	None
MeC. II.	..		12/18/09 a. m.	L. A.	+	1022	V. S. T. nucleo	None	None
.....	..		1/20/10 p. m.	L. A.	+	1027	None	None	None
.....	..		12/18/10 m.	L. A.	+	1024	None	None	Calc. oxalate
K. II.	12		12/19/10 m.	L. A.	+	1020	V. S. T. nucleo	Indican	None
.....	..		11/ 1/09 a. m.	L. A.	+	1018	None	None	Calc. oxalate
.....	..		11/ 2/09 a. m.	L. A.	+	1018	None	None	None
.....	..		11/ 3/09 a. m.	L. A.	+	1020	V. S. T. nucleo	None	Uric acid; calc. oxalate
.....	..		11/ 4/09 a. m.	L. A.	+	1020	S. T. nucleo; S. T. serum	Indican	Uric acid; calc. oxalate
.....	..		11/ 5/09 p. m.	L. A.	+	1024	V. S. T. nucleo; V. S. T. serum	Indican	Uric acid
.....	..		11/ C/09 a. m.	L. A.	+	1024	None	None	Hyaline; cylindroid; ammon. urate; calc. oxalate

TABLE 3.—(CONTINUED)

Name	Age Yrs.	Am't c. c.	Date	Color	Reaction*	Spec. Grav.	Albumin ^g	Indican, Urobilinogen, Phenol	Casta, Cylindroids, Crystals
.....	..		11/ 7/09 p. m.	L. A.	+	1018	V. S. T. nucleo	None	Calc. oxalate
.....	..		11/ 8/09 a. m.	L. A.	+	1020	None	None	Uric acid; calc. oxalate
.....	..		11/ 9/09 a. m.	L. A.	+	1020	V. S. T. nucleo; V. S. T. serum	None	None
.....	..		11/10/09 a. m.	L. A.	+	1020	None	None	Earthy phosph.
.....	..		11/12/09 a. m.	L. A.	+	1020	V. S. T. nucleo	None	Uric acid
K. T.	..	1950	11/15/09 t.	L. A.	+	1018	None	None	None
.....	..		11/15/09 p. m.	L. A.	+	1023	None	Indican	None
.....	..		11/16/09 p. m.	L. A.	+	1028	V. S. T. nucleo; V. S. T. serum	None	None
.....	..		11/17/09 a. m.	P.	+	1020	V. S. T. nucleo; V. S. T. serum	None	Uric acid
.....	..		11/17/09 p. m.	P.	+	1030	V. S. T. nucleo; V. S. T. serum	None	Amorph. urates
.....	..		11/18/09 p. m.	P.	+	1030	V. S. T. nucleo	None	Hyaline cylindroid
.....	..		11/18/09 a. m.	A.	—	1024	None	None	Earthy phosph.
.....	..		11/19/09 p. m.	A.	+	1028	V. S. T. nucleo	None	Amorph. urates; calc. oxalate
.....	..		11/20/09 a. m.	L. A.	+	1030	S. T. nucleo	None	Ammon. urates; calc. oxalate
.....	..	1875	11/22/09 t	A.	+	1020	None	None	Calc. oxalate
.....	..		11/23/09 a. m.	L. A.	+	1022	V. S. T. nucleo	Phenol	Uric acid
.....	..		11/24/09 a. m.	A.	+	1025	V. S. T. nucleo	Not exam.	Cylindroid
.....	..		11/26/09 m.	L. A.	+	1030	S. T. nucleo	Not exam.	Cylindroid
.....	..		11/27/09 a. m.	L. A.	+	1024	V. S. T. nucleo	None	Uric acid
K. H.	..		12/ 2/09 m.	L. A.	+	1027	V. S. T. nucleo	None	Hyaline; cylindroid; uric acid; calc. oxalate
.....	..		12/ 2/09 p. m.	L. A.	+	1022	None	None	Uric acid; calc. oxalate
.....	..		12/ 4/09 a. m.	L. A.	+	1026	None	None	None
.....	..		12/ 6/09 m.	L. A.	+	1024	V. S. T. nucleo	None	Not exam.
.....	..		12/ 6/09 a. m.	L. A.	+	1026	V. S. T. nucleo	Indican; phenol	None
.....	..		12/ 6/09 p. m.	L. A.	+	1022	V. S. T. nucleo	None	None
.....	..		12/ 8/09 p. m.	D. A.	+	1030	V. S. T. nucleo	None	None
.....	..		12/ 9/09 a. m.	L. A.	+	1022	V. S. T. nucleo	None	Not exam.
.....	..		1/ 7/10 a. m.	L. A.	+	1020	V. S. T. nucleo	None	None
.....	..		2/14/10 p. m.	A.	+	1026	V. S. T. nucleo	None	None

state of our knowledge regarding the nature of this latter body, we have used for its description the term nucleo-albumin.

The proportions of the different albumins present in these 124 children were as follows: thirty-four, or 27.4 per cent., showed serum-albumin—alone (four) and in combination (thirty); and in 106, or 85.4 per cent., nucleo-albumin—alone (seventy-six) and in combination (thirty). In other words, this so-called nucleo-albumin was present three times as often as serum-albumin.

We are convinced that these figures do not fairly represent the frequency of occurrence of either of these albumins. This statement is based on the following facts: In Group 1, there were thirty-eight children from whom we examined but one sample. In this number nucleo-albumin was present twenty-five times, equalling 75.8 per cent. as compared with 85.4 per cent. for the total number of children, and 94.7 per cent. for thirty-eight children from whom we made examinations of the twenty-four-hour quantity.

In this same group of thirty-three children, serum-albumin was present seven times, which was equal to 21.2 per cent. as compared with 27.4 per cent. for the total number, and 42.1 per cent. for the thirty-three children from whom we made examinations of the twenty-four-hour quantity.

We are inclined to believe that had we examined not only the twenty-four-hour quantities, but also a number of samples voided at different hours of the day and continued these examinations over a period of days, we might have been able not only to demonstrate the presence of nucleo-albumin at some period in the urine of every child examined, but also to have increased the percentage of cases showing serum-albumin. In the one child in whom we failed to find either form of albumin in the twenty-four-hour specimen (a child in Group 4) nucleo-albumin was frequently found in the daily examinations and serum-albumin occasionally.

Believing, therefore, that it is possible to demonstrate in the urine of every presumably healthy child traces of an albuminous body precipitated by acetic acid, we are naturally forced to the conclusion that its presence cannot necessarily be considered an indication of a lesion of the kidneys, and that it must, therefore, be regarded as an exceedingly common, if not constant manifestation in the urines of children under 14 years of age, and that it is consequently of no clinical significance.

As to the interpretation of the serum-albumin we believe that the cause suggested for the occasional presence of casts and cylindroids is quite sufficient to account for its occurrence in the amounts in which it has been present in the urines we have examined, for it must be borne in mind that in all of our cases neither the nucleo- nor serum-albumins have ever been present in more than traces and in the vast majority, only in very slight traces.

SUMMARY

1. There has been no relationship between the specific gravity and the form or amount of albumin.

2. The reaction has had no influence on the production of albumin.

3. Sugar, acetone, and diacetic acid were never found. They may, therefore, be considered as having no bearing on the production of albumin.

4. Indican, phenol, and urobilinogen when present were usually associated with albumin, but albumin was sometimes absent when they were all present, and the amount was never greater when associated with them than it was in the cases in which they were absent.

5. Crystals, when present in amounts, such as are occasionally found in normal children, are in no way responsible for the associated albumin.

6. The mild disturbances of the intestinal digestion, as shown by the examination of the stools, were not sufficient to account for the occurrence of albumin.

7. The blood-pressure was within the normal range in all cases and, therefore, did not influence the albumin output.

8. The albumin elimination was the same on mixed and exclusive milk diets.

9. We found no children in whom the albumin excretion corresponded to the requirements for postural or orthostatic albuminuria, a rather surprising result in view of the frequency with which this condition is supposed to occur.

10. Thirty-two and one-half per cent. of the children showed occasional hyaline casts and cylindroids in their urines. We do not consider their "occasional presence" as indicative of a lesion of the kidneys, but rather as suggesting a temporary overtaxation of the kidneys resulting from variations in the habits of life of the individuals which are too slight to be recognized.

11. Eighty-eight and seven-tenths per cent. of the urines of these 124 children showed albumin, 27.4 per cent. showing serum-albumin alone, and in combination; and 85.4 per cent. an albuminous body precipitated by acetic acid in the cold. These two albumins were nearly always present in very slight traces, occasionally in slight traces and rarely in traces.

In thirty-eight children the twenty-four-hour specimens showed nucleo-albumin in all but one, and in this case samples examined over prolonged periods of time showed nucleo-albumin frequently.

In these thirty-eight children, the percentage of serum-albumin was very much higher (42.1 per cent.) than in the total number of cases examined. We believe, therefore, that it is possible to demonstrate in

the urine of every presumably healthy child, traces of an albuminous body precipitated by acetic acid. Consequently, this substance must be regarded as an exceedingly common, if not constant manifestation in the urine of children under 14 years of age, and as of no clinical significance.

We do not believe that serum-albumin in the amounts in which it appears in these children indicates a diseased condition of the kidneys any more than does the presence of occasional hyaline casts and cylindroids, and that its etiology may be considered the same as that given for these former elements.

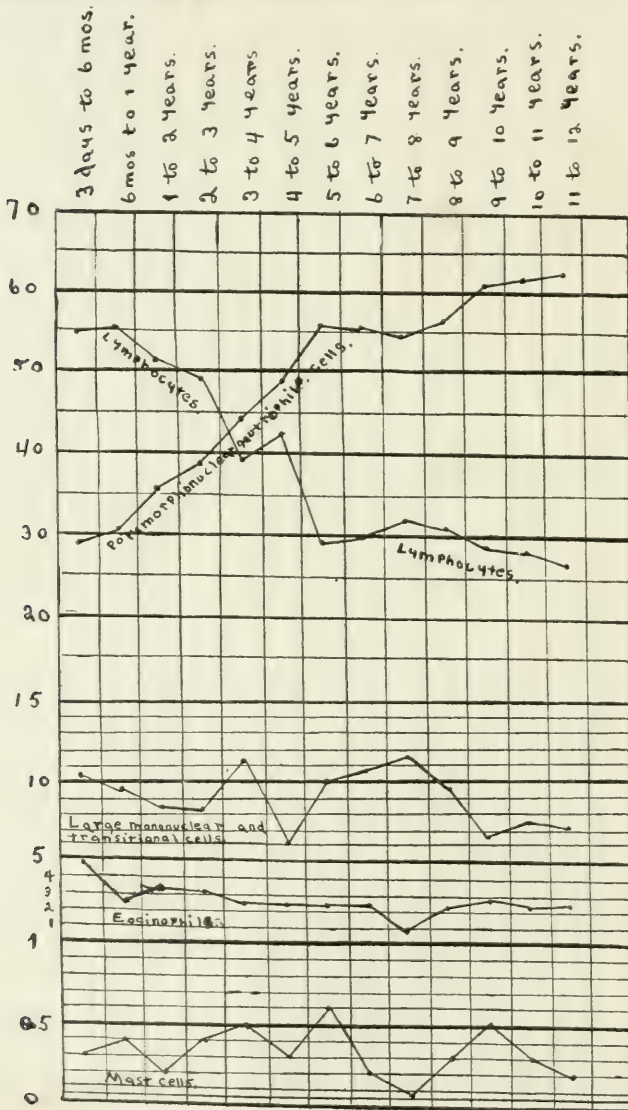
PROGRESS IN PEDIATRICS

ANATOMY AND PHYSIOLOGY

Normal Percentages of Leukocytes in Infants and Children

(O. M. Schloss. *Arch. Int. Med.*, 1910, vi, 638)

A series of differential blood-counts were made by Schloss on eighty apparently normal infants and in children between 3 and 12 years of age. The investigation was undertaken primarily to determine, if possible, the normal percentages of the



Differential percentages of the leukocytes during the first twelve years of life.

cells with eosinophilic granules. Most of the children were from the poorer classes, but all cases of manifest illness were excluded. Cases were also excluded in which there was a history of any disease recognized as a cause of eosinophilia. The following precautions were taken in the attempt to eliminate helminthiasis: The counts on children between 1 and 12 years of age were made only in instances in which the history and a previous examination of the feces were negative. In infants under 1 year of age, the feces were examined in cases showing more than 5 per cent. of eosinophil cells. The eosinophil cells were over 6 per cent. in seven of fifteen infants under 2 months of age; the highest percentage was 9.7. In two additional cases the percentage was greater than 5; in one, 5.2 per cent.; in another, 5.3 per cent. The highest percentages were found in infants between 2 days and 2 weeks of age. In none of the fifty-five infants and children between 2 months and 12 years of age was the percentage of the eosinophil cells above 6. In two cases the eosinophil cells were 6 per cent. In all other cases the percentage was less than 5. In apparently normal infants from 3 days to 2 months of age, the eosinophil cells were frequently above the percentages normal for adults. In normal individuals between 2 months and 12 years of age, when the known causes of eosinophilia were excluded, the eosinophil cells were rarely above 5 per cent. and never greater than 6 per cent., and were present in approximately the same relative proportion as in adults. It therefore only seems fair to conclude, says Schloss, that there is no physiologic eosinophilia in childhood; that 5 per cent. of eosinophil cells may be considered as the upper limit of normal, and certainly, more than 6 per cent. as pathologic.

F. ZAFFEE.

BACTERIOLOGY AND PATHOLOGY

Anti-Infectious Power of the Blood of Infants

(*Ruth Tunnickliff. Jour. Infect. Dis., 1910, vii, No. 5, p. 698*)

The results of Tunnickliff's experiments would indicate that at birth the opsonic power of the blood-serum toward streptococci, pneumococci, and staphylococci is a little less than that of the adult serum. It falls still lower during the first months of life and does not equal the opsonic power of adult serum until about the second year. The phagocytic activity of the leukocytes of infants toward streptococci, pneumococci, and staphylococci follows a course similar to that of the opsonic indices. The leukocytes at birth are a little less active than adult leukocytes. Their activity diminishes considerably during the first months of life and does not reach that of adult leukocytes until about the third year. The phagocytic power of the whole blood of infants drops decidedly during the first and second months of life and does not reach that of adult blood until about the third year. During the first and second years of life the anti-infectious power of the blood, as measured by the opsonic power of the serum and the phagocytic power of the leukocytes, is far below that of adult blood.

F. ZAFFEE.

Method of Staining Capsulated Bacteria in Body Fluids

(*William H. Smith. Boston Med. and Surg. Jour., 1910, cxliii, 791*)

The author has used the following method with good results in staining bacteria with capsules: (1) Make a thin smear from fresh sputum, lung, pleural or pericardial exudate. (2) Pass through flame. (3) Cover with 10 per cent. aqueous solution of phosphomolybdic acid (Merek) four to five seconds. (4) Wash in water. (5) If the organism is gram-staining, stain with anilin oil gentian violet, steaming one-quarter to one-half minute. (6) Wash in water. (7) Treat with Gram's solution of iodine, steam one-quarter to one-half minute. (8) Decolorize with 95 per cent. alcohol. (9) Wash in water. (10) Stain with 6 per cent. aqueous solution of eosin one-half to one minute, warming gently. (11)

Chlorids in Stomach Contents of Infants

(A. H. Wentworth, *Boston. Arch. Int. Med.*, 1910, vi, p. 617)

The observations recorded in Wentworth's paper are a continuation of work briefly alluded to in a previous article. The purpose of this work is to discover whether or not the hydrochloric acid of the gastric juice is diminished in cases of infantile atrophy. In the first series of observations, the stomach contents were obtained one hour after eating, from a limited number of atrophic infants fed on mixtures of cow's milk. The determinations were made by Sjöquist's method. The results showed a diminished amount of hydrochloric acid in the stomach contents in every case. The same series of observations included determinations of hydrochloric acid in the stomach contents from a limited number of well-nourished and apparently healthy infants fed on mixtures of cow's milk. The results in these cases were variable. In four cases the amount of hydrochloric acid was much greater than in the cases of atrophy. In three cases the amount of hydrochloric acid approximated that of the atrophic infants. As these results were not conclusive, a second series of observations was made with a view to controlling the first series. The same method of analysis was employed. Unfiltered stomach contents were used in every case. The diagnosis of infantile atrophy was made from clinical evidence alone. Most of the cases were under observation for several weeks. The Sjöquist method rarely showed more than a trace of hydrochloric acid in the stomach contents from atrophic infants fed on cow's milk mixtures. Out of twenty-one determinations made of hydrochloric acid in the stomach contents, obtained from eight infants, ten showed a percentage of hydrochloric acid between 0.01 and 0.05, and eleven showed a percentage of hydrochloric acid between 0.002 and 0.009. The stomach contents from nine well-nourished infants showed a diminished amount of hydrochloric acid. The diminution of hydrochloric acid corresponded closely with that found in about one-half of the determinations made on the above mentioned atrophic infants. Out of twelve determinations of hydrochloric acid in the stomach contents obtained from nine infants, one showed 0.12 per cent., one showed 0.09 per cent., nine showed percentages between 0.01 and 0.05; and one showed 0.005 per cent. hydrochloric acid. Thus the diminution of hydrochloric acid, although it was marked, was never so extreme as in one-half of the determinations obtained from atrophic infants. Examinations of the stomach contents obtained from the same atrophic infants at different periods of time after eating, and without any change in the diet, rarely showed any marked variations in the quantity of hydrochloric acid present. Wentworth does not believe that the results of these observations prove that a marked diminution of hydrochloric acid in the gastric juice is an essential factor in the production of infantile atrophy, although they do show that this diminution is constant. On the other hand, considerable evidence is afforded by several of the observations that it is possible for atrophic infants to gain very rapidly in weight and yet produce very little hydrochloric acid in the gastric juice. This appears to show that the quantity of hydrochloric acid in the gastric juice is not an important factor in recovery from infantile atrophy.

F. ZAPFFE.

ACUTE INFECTIOUS DISEASES**Cutaneous Diphtheria**

(Edwin H. Place, *Boston Med. and Surg. Jour.*, 1910, clxiii, 730)

The author reports a case of primary cutaneous diphtheria in a child of 7 months, involving the skin of the lower third of the abdomen, anterior portion of the buttocks, vulva, perineum and internal surface of the thighs. The lesion consisted in swelling, redness and a grayish hyaline membrane firmly adherent, which if removed left behind a granular bleeding surface. There was no known exposure to diphtheria and the child had no evidence of disease elsewhere.

There was a previous eczema of the pubic region and the infection with diphtheria was probably implanted on this by the hands of some attendant. The case resulted fatally despite the administration of antitoxin. The diagnosis was proved by culture and animal inoculation.

RICHARD M. SMITH.

Malaria Spread Through Other Agencies than the Mosquito

(*Jesus Chico. Am. Jour. Pub. Hyg., 1910, xx, 561*)

The undoubted presence of malaria in Guanajuato, Mexico, has frequently been shown by finding the plasmodium in the blood of patients. It is equally sure that there are no anopheles mosquitoes in the district. Since 1882 malaria has been much severer in character than formerly and the cases more numerous. *Culex* mosquitoes came to Mexico in 1888, but there was no increase in malaria as a consequence. Despite careful search no connection has been found between malaria and the *culex* mosquito. Communication with the coast cities is much easier and therefore more intimate than formerly. Fresh fruits brought from the coast are considered as the vehicle, and to account for the increase in the disease since 1882.

RICHARD M. SMITH.

Contribution of Experimental to Human Poliomyelitis

(*S. Flexner, New York. Journal A. M. A., Sept. 42, 1910*)

Flexner gives a résumé of the experimental contributions to our knowledge of human poliomyelitis. These he shows have yielded a number of important facts relating to the spontaneous disease in man. These facts include the discovery of the nature of the virus, of many of its properties, of certain important clinical and pathological peculiarities of this disease, of the phenomena of immunity, of a mode of spontaneous infection through the nasopharyngeal mucosa, and have also served as a basis on which to develop measures of prevention, and on which it is hoped to work out a successful treatment. The advances which have been made will make it possible to accurately determine whether the disease is a single clinical and pathologic entity or whether it is a generic name covering groups of symptoms and due to the effects of certain lesions of the brain and cord, of which it is not merely one, but the most important, variety. It is not improbable he says that poliomyelitis, like meningitis, may be found to rise from several independent causes and that epidemic poliomyelitis, like epidemic meningitis, may be distinguished among the varieties by being always the result of a particular microorganism. We have already evidence that certain animals like the dog, poultry, and possibly the horse, are subject to poliomyelitis due to a special germ in each case.

H. M. BANNISTER.

Clinical Features of Epidemic Poliomyelitis

(*L. E. Holt. Arch. Pediat., 1910, xxvii, 641*)

Giving a brief history of the epidemics of the past five years, Holt says that it is hardly conceivable that such epidemics of poliomyelitis as have been recorded could previously have been passed over without recognition, and he believes that a wave of infection, starting apparently from Scandinavia, is gradually spreading over this country, possibly over the world. Briefly summarized, the recent epidemics were as follows:

1905 and 1906, Scandinavia, 2 epidemics, with total cases.....	1,053
1907, New York City and vicinity, total cases.....	2,000
1907, 11 other epidemics, with total cases.....	349
1908, 8 epidemics, with total cases.....	520
1909, 9 epidemics, with total cases.....	1,018

Holt believes there is no difference between the sporadic and the epidemic forms of the disease, except possibly in communicability and severity. The analogy to cerebrospinal meningitis is a very close one. Epidemics thus far reported have occurred invariably in the summer, but sporadic cases, though

more frequent in the summer, are observed throughout the year, and the identity of the two forms would seem to be demonstrated by the experiments on monkeys by Flexner, who transferred the disease from the organs of such a sporadic winter case. It would appear from statistics that the virulence of the infective agent is greater when the disease is epidemic, and this may explain the higher mortality and the greater communicability. In the Nebraska epidemic it was noted that the cases were more severe and the mortality higher in the latter part of the epidemic. The Massachusetts reports for 1907 showed the mortality in 234 scattered (sporadic form) cases to have been 5 per cent. The mortality in 1,659 cases in epidemics, previously reported by Holt, was 12 per cent. In fourteen more recent, localized epidemics, representing 1,209 cases, the mortality was 12.3 per cent. This correspondence Holt thinks is striking. A difference of opinion among observers as to whether the abortive forms should be included in the statistics vitiates to an extent the mortality percentage, but in various epidemics it has ranged from 6 to 20 per cent., averaging about 12 per cent. In sporadic cases the mortality is certainly much lower. The existence of abortive cases has been confirmed by the epidemics in New York, in Scandinavia and in other localities. The symptoms of this form while fairly uniform are not sufficiently characteristic to make the diagnosis when the cases are seen by themselves, and when occurring sporadically would hardly be suspected. The onset is usually abrupt, with vomiting; there is constipation and fever, from 101 to 103 F., hyperesthesia, pains in the back and neck, and sometimes stiffness of the neck. Prostration may be sufficient to keep the child in bed. The symptoms subside in two or three days and there is complete recovery. Holt believes that the reports of the epidemic in Tröstena, Sweden, and that at York, Nebraska, as well as some others, afford striking confirmation of the communicability of the disease. It seems to Holt to be conclusively shown that the disease under certain conditions is highly contagious, demanding during an epidemic strict quarantine. It is almost conclusive that healthy persons may be carriers of the disease, and that this may take place for a considerable time after contact with active cases, but there is no evidence of any other medium of contagion than those suffering with the disease or those exposed to it. A better understanding of the pathology suggests that a better term would be epidemic myelitis or epidemic myeloencephalitis.

J. B. CHAMPION.

Should Epidemic Poliomyelitis be Quarantined?

(G. P. Shidler. *York, Nebraska*)

Shidler in reviewing the literature of epidemics of poliomyelitis, and especially the Nebraska epidemic of 1909, reaches the conclusion that poliomyelitis is highly contagious and should be strictly quarantined. Taking a list of sixty Nebraska cases as they occurred and ten other instances in which there was but a single case in a family of more than one child, he found that:

"Thirty-four per cent. of cases occurred as single cases in families having more than one child; 44 per cent. occurred in families in which there were two or more children, all of whom acquired the diseases; 4 per cent occurred in families in which there was but the single child; 64 per cent. occurred in families in which there was more than a single child in the family affected. In forty-one families with a total of 150 children, eighty-six children, or 57 per cent., contracted the infection."

HENRY F. KEEVER.

SYPHILIS AND TUBERCULOSIS

Results with v. Pirquet's Cutaneous Reaction and with the Injection or de-Pot Reaction

(*Nothmann. Arch. f. Kinderh., 1910, liii, Nos. 1-3, p. 146*)

In a series of children at the Düsseldorf Clinic for Pediatrics, Nothmann compared the results obtained with two different tuberculin tests—the v. Pirquet

test, and the injection test, giving the so-called dePot reaction. This consists in a subcutaneous thickening, sometimes accompanied by a reddening of the skin, at the site of the injection of a dose of highly diluted tuberculin so small that no generalized reaction occurs. In this series of cases a v. Pirquet test was performed on all; on those who showed no reaction after a week a second test was made; while to those who still showed no reaction, an injection of 1 c.c. of a 1-1000 solution of tuberculin was given. If there was no reaction at first the dose was increased. The results were as follows: 47.1 per cent. gave positive reactions after the first v. Pirquet test; 18.6 per cent. more gave a positive reaction at the second test, making 65.7 per cent. positive altogether; 11.3 per cent. more gave positive dePot reactions, giving a total 77 per cent. positive from all the tests. He also studied the disappearance of the v. Pirquet test in acute diseases. He considers that its disappearance in measles may be used as a point in diagnosis; and he found that it disappeared sometimes in the course of croup-pneumonia.

G. L. MEIGS.

Tuberculosis of the Ankle-Joint

(J. W. Sever, Boston. Jour. Am. Med. Assn., Dec. 17, 1910)

Sever notices the comparative frequency of tuberculosis of the ankle, it being greater than that of cases of tuberculosis of the elbow or shoulder joint in children. Boys seem to be more subject to it than girls, owing probably to their greater liability to trauma. A tuberculous family history is important, and about a fourth of the 213 cases observed in the Children's Hospital, Boston, since 1868 had other joints involved. The cases were usually of considerable duration when received, owing probably to irresponsibility of parents and mistaken diagnoses of sprains, etc. The onset is usually slow and the most frequent location of the disease is the astragalus, the os calcis coming next. The cardinal symptoms are pain, soreness, limp, swelling and muscle spasm. Chronic sprain, irritable flat-foot, syphilis and infectious arthritis are to be ruled out by the history. The pathology is like that of all other bone tuberculosis. The treatment is operative and non-operative. The first thing is to prevent weight-bearing and to enforce rest, improve the general health, give plenty of restful outdoor life and nourishing food. Sever thinks there is a distinct advantage, in children at least, in a conservative plan of treatment. Radical operations on the joints and bones of children are not the best methods of treatment and are only indicated when everything else has failed to stop the progress of the disease. When operations are done they should be clean. No curetting should be allowed, and any bone or bones involved should be removed *in toto* with as little mutilation as possible. In any case there may be deformity needing correction after a cure which can be done by appropriate tenotomies or osteotomies, a sufficiently long time having elapsed to avoid any further lighting up of the original disease. The conclusions are summarized as follows: Tuberculosis of the ankle-joint and bones of the foot in children is insidious in its onset, chronic in its course, and attacks usually young children. The expectant or conservative method of treatment is preferable to the operative one. Time is saved and deformity less under the conservative plan than by the operative method. There is also less danger of secondary joint involvement and general tuberculosis by pursuing the non-operative plan. The disease may be associated with bone and joint tuberculosis in other parts of the body. The prognosis is fairly good for life, but poor for a good ankle-joint in which there is no disability. A certain number get a good functional ankle, with but slight deformity. In regard to the smaller metatarsal bones the results are good for joint motion.

H. M. BANNISTER.

RESPIRATORY SYSTEM

Pneumothorax

(*James B. Ayer. Boston Med. and Surg. Jour., 1910, clxiii, 501*)

Ayer analyzes seventy-two cases of pneumothorax which have occurred at the Boston City Hospital since 1900, when the cases for the previous fifteen years were analyzed by Morse. During the twenty-eight years covered by the reports, 69 per cent. of the cases were in tuberculous patients. Most of them had a history of less than six months' illness. Pain and dyspnea were the most common symptoms of onset. The opening from the lung into the pleural cavity is very small and occurs on the side of the most rapidly advancing process. Pneumothorax may follow long standing empyema. The onset in these cases does not usually show acute symptoms. Operative treatment is frequently permanently successful. In traumatic cases fluid develops rapidly; the air does not last long and is of no serious import. Two rare causes—echinococcus and subphrenic-intra-thoracic abscess—are reported. Nineteen per cent. and possibly 32 per cent. of the whole series were artificially produced. This percentage is too large and could be largely avoided by the use of a simpler and safer instrument in tapping. X-ray examination is of great use in diagnosis and prognosis, and in explaining the effect of treatment.

RICHARD M. SMITH.

GENITO-URINARY SYSTEM

Bacterial Vaccines in Pyogenic Infections of the Urinary Tract

(*H. F. Hartwell. Boston Med. and Surg. Jour., 1910, clxiii, 472*)

The results of the use of vaccines in twenty-five cases of pyogenic infection of the urinary tract at the Massachusetts General Hospital are reported. The colon bacillus was the organism present in almost all of the cases. In females, in whom pyelitis or pyonephritis is the common lesion, the cases are essentially chronic, with exacerbations of acute symptoms. Vaccines had no effect in lessening the amount of pus or bacilluria or in preventing the acute exacerbations. In acute and subacute infections of the kidney pelvis, vaccines seem to offer promising results. Cases of nephrotomy with drainage were not influenced in any way by vaccines. In mild cases of bladder infection the irritation, frequency of urination and pain diminished steadily with treatment. Bacilluria was obstinate. Severe cases of cystitis were not benefited by vaccines.

RICHARD M. SMITH.

EYE, EAR, NOSE AND THROAT

Torticollis After Removal of Adenoids of Nasopharynx

(*J. Weinstein. Pediatrics, 1910, xii, 762*)

Weinstein reports two cases of torticollis following adenectomy at Scheier's Poliklinik, Berlin. In each case the contraction of the sterno-cleido-mastoid muscle appeared three days after the operation, with much pain on moving the head. The symptoms disappeared entirely by the fifteenth day. He attributes the cause to trauma of the sterno-cleido-mastoid muscle.

HENRY F. KEEVER.

PHYSIOLOGY AND PATHOLOGY OF THE DIGESTION OF FAT IN INFANCY

THEIR APPLICATION TO INFANT-FEEDING *

FRITZ B. TALBOT, M.D.

BOSTON

The food of infants comes in the main from two sources, human milk and cows' milk, the former being the natural food and the latter the best substitute we have when the former supply fails us. A brief description of these two milks is necessary for a clear conception of the subject.

The percentage of fat in cows' milk varies with the individual cow and the species. The milk of the ordinary grade cow, the Holstein or Ayrshire, contains 4 per cent. or less of fat, and that of the Jersey or Guernsey 4 per cent., or more, of fat. The fat is held in a coarser emulsion and separates more easily than that of human milk. There are other differences in the chemical and physical composition of the two milk-fats, but these will not be taken up in this paper.

Human milk normally contains, in round numbers, about 4 per cent. of fat; this percentage, however, may vary considerably in pathologic conditions, the extremes being 0.1 per cent.¹ and 13.7 per cent.² Every woman has a certain amount of fat to secrete in her milk, and, under like conditions, gives the same total day by day. The percentage of fat in the milk gradually increases in a certain definite curve from the beginning to the end of each nursing, the smallest percentages coming at the beginning and the highest at the end.² For example, the first part of the milk usually contains 2 per cent. of fat, and the last part 6 per cent. of fat; and the mixture of the whole amount of milk secreted in a single breast contains 4 per cent. of fat. The amount of milk secreted does not influence this curve otherwise than by making the ascent rapid or

* Read in the Section on Diseases of Children of the American Medical Association, at the Sixty-first Annual Session, held at St. Louis, June, 1910.

1. Moll: Ueber Fettvermehrung der Frauenmilch durch Fettzufuhr, nebst einem Beitrag für die Bedeutung der quantitativen Fettunterschiede für das Gedeihen der Brustkinder, Arch. f. Kinderh., xlviii, 161.

2. Forrest, M.: Ueber die Schwankungen im Fettgehalte der Frauenmilch und die Methodik der Milchentnahme zu Fettbestimmung, Arch. f. Kinderh., xlii, 1.

3. Engel: Ueber die Quellen des Milch und Colostralfettes und über die bei der Milchsekretion wirkenden Kräfte, Arch. f. Kinderh., xliii, 194 and 204.

gradual.⁴ Occasionally there is more fat in the first part of the milk than in the last part and the curve is just the reverse of the one just described.⁵

It is probable that the body-fat as well as the food-fat may be the source of milk-fat,⁶ but it is not clear how the fat can be obtained from this source. Thiernich examined the literature on the influence of food on the quantity of fat secreted in the milk and came to the conclusion that a fat-free diet not only changed the quality of the fat, but also caused at the same time a diminution in the amount of fat in the milk. When a person is underfed, an increase in the fat in the food results in an increase in the fat in the milk,⁷ but when large amounts of fat are added to a normal diet there is only a temporary increase in the amount of fat in the milk despite the excess of fat in the diet.⁸ Ebstein⁹ found in his clinic that many women with a fat-poor breast-milk would secrete more fat if they were given more fat in the food.

The amount of fat ingested by infants naturally depends on the amount in the milk, the amount of milk taken, and the part of the milk given. In asylums where one wet-nurse feeds two or more babies, the baby nursed first gets a milk relatively low in fat and the last one a milk relatively high in fat (possibly 6 per cent.). This fact is of great practical importance in feeding very delicate or sick babies, which are unable to digest large amounts of fat of any sort. Such babies may be given the first part of the milk which comes from the breast, or if desired skimmed drawn breast-milk. The wet-nurse is always instructed to nurse the sick baby first, and her own baby last; one of the reasons is that the sick baby does better on the weaker milk. In general, the amount of milk which

4. Aurnhammer: Ueber die Beziehungen zwischen Milch production und Fettgehalt der Milch, *Arch. f. Kinderh.*, 1909, li, 160.

5. Engel: Zur Methodik der Fettbestimmung in der Frauenmilch und die Methodik der Milchentnahme zu Fettbestimmungen, *Arch. f. Kinderh.*, 1906, xliii, 181.

6. Bendix: Ueber den Uebergang von Nahrungsfetten in die Frauenmilch, *Deutsch. med. Wchnschr.*, 1888, No. 14; Thiernich: Ueber den Einfluss der Ernährung und Lebensweise auf die Zusammensetzung der Frauenmilch, *Monatschr. f. Geburtsch. u. Gynäk.*, 1899, ix, No. 4; Gogitidse: Vom Uebergang des Nahrungsfettes in die Milch, *Ztschr. f. Biol.*, xlv, 353; *ibid.*, xlv, 403; Caspari: Ein Beitrag zur Frage nach der quelle des MilCHFettes, *Arch. f. Anat. u. Physiol. (Suppl.)*, 1899, 267; Engel: Ueber das MilCHFett Stillender Frauen bei der Ernährung mit spezifischen Fetten, *Wien. klin. Wchnschr.*, 1906, No. 29, p. 898.

7. Johannessen: Studien zur Sekretionsphysiologie der Frauenmilch, *Jahrb. f. Kinderh.*, xxxix, 380.

8. Albert, F.: Ueber den Einfluss von Fettfütterung auf die Milchmenge und den Fettgehalt der Milch, *Ref. Malys Jahresbr. f. Tierchemie*, xxix, 253; Henriques and Hansen: Untersuchungen über die Fettbildung im Tierorganismus nach intensiver Fettfütterung, *Malys Jahresbr. f. Tierchemie*, xxix, 68.

9. Ebstein: Die Verdauungsstörungen im Säuglingsalter, *Ebstein-Schwalbes Handb. d. prakt. Med.*, 1900, ii, 299.

a baby will take decreases, the richer it is in fat.¹⁰ This, however, does not usually hold true of sick babies, because the amount of milk they take in twenty-four hours does not increase with the lowered percentage of fat, but only with the return to health.¹ Therefore, when a baby has an acute infection, such as pneumonia, the milk mixture should be diluted as a whole; the fat should not be removed entirely from the mixture, because it has twice as much food value as either the sugar or protein, and because in such cases the presence or absence of fat does not influence the amount of milk taken. If, on the other hand, a healthy infant is given 5 per cent. or more of fat in its food, it will usually take less and less, and if the amount of fat is diminished it will eat more. Many babies get 6, 10 and even 12 per cent. of fat in the food because the milk mixtures are prescribed ignorantly or made improperly. This could be avoided by estimating the amount of fat in the milk by the Babcock method. When normal babies are upset by fat, it is the rule rather than the exception to find that they are receiving more than 5 per cent. in the food.

PHYSIOLOGY

The physiology of the digestion of fat is not simple, but certain facts have been established which throw some light on what is happening to the fat in the gastro-intestinal canal.

STOMACH DIGESTION

The motility of the stomach is influenced by many things, such as the concentration and the character of the food.¹¹ Nothing has so much influence on the time required to empty the stomach as variations in the amounts of fat, which delay or hasten the evacuation of food into the duodenum. When there is a large amount of fat in the food, the food is kept in the stomach longer, and when a small amount, a shorter time.¹² According to some writers,¹³ the stagnation of fat has a connection with the pathologic condition of pyloric stenosis. It has been demonstrated in animals that fat delays the secretion of hydrochloric acid. Cannon has shown that the cardiac orifice remains open as long as the reaction of the cardia is alkaline; as soon as the reaction becomes acid, the cardiac orifice closes and remains so until the neighboring food components become alkaline. The pyloric valve acts in a manner directly

10. Gregor: Der Fettgehalt der Frauenmilch und die Bedeutung der physiologischen Schwankungen desselben in bezug auf das gedeihen der Kinder, Samml. klin. Vort. von Volkmann, 1901, No. 302.

11. Clark: Am. Jour. Med. Sc., May and June, 1909.

12. Tobler and Bogen: Ueber die Dauer der Magenverdauung der Milch und ihre Beeinflussung durch verschiedene Factoren, Monatschr. f. Kinderh., vii, 12.

13. Tobler: Beobachtungen über die Zusammensetzung des Mageninhalts bei kongenitaler Pylorusstenose, Verhandl. d. Gesellsch. f. Kinderh., 1907, p. 411.

opposed to that at the cardia. When the material in the antrum pylori is acid, the valve opens and *vice versa*.¹⁴

These two facts may be applied clinically in explaining regurgitation due to too much fat in the food. Fat delays or inhibits the secretion of hydrochloric acid, and the cardiac sphincter, or lid to the stomach, remains open so that milk can be pushed back into the esophagus by the peristaltic movements of the stomach. If the amount of fat in the food is diminished, regurgitation stops, presumably because the normal amount of hydrochloric acid is again secreted, causing the entrance to the stomach to close and the outlet to open at the proper time.

It has been assumed until recently that only the pancreatic juices contain fat splitting ferments. Sedgewick¹⁵ found a ferment in the stomach contents of infants which is capable of splitting in the test-tube one-fourth of the fat, and in the body about 12 per cent. of the fat ingested. Ibrahim¹⁶ found this same ferment in the mucous membrane of the stomach of both the fetus and the new-born baby, and proved conclusively that there is a very powerful fat-splitting ferment which in a 9-months old baby that had died from pneumonia split in twenty-four hours over 40 per cent. of the fat in the yolk of an egg.

Nature, however, provides that too much fat shall not be set free in the stomach at one time. This is brought about in the following manner: When the casein of milk is coagulated in the stomach, practically all the fat is entangled in its meshes. The casein surrounding it must be digested before any more fat can be reached by the digestive juices, and thus only as much fat is set free as the progress of digestion warrants.

INTESTINAL DIGESTION

When the stomach digestion is complete, the food is discharged into the duodenum accompanied by organic or inorganic acids which start the secretion of the pancreatic juice and bile.¹⁷ Ibrahim¹⁸ substantiated Zweifel's¹⁹ findings that the pancreas of the fetus contains a fat-splitting ferment and that the action of this ferment is increased materially by the

14. Cannon: Am. Jour. Physiol., 1908, xxiii, 105.

15. Sedgewick: Die Fettspaltung im Magen des Säuglings, Jahrb. f. Kinderh., 1906, lxiv, 194.

16. Ibrahim, J., and Kopec, T.: Die Magenlipase beim menschlichen Neugeborenen und Embryo, Ztschr. f. Biol., München., 1909, liii, 201.

17. Baylies and Starling: Jour. Physiol., 1902, xxviii, 325; 1903, p. 174.

Laqueur: Sur la présence et la localisation de la sécrétine dans l'intestin du nouveau-né et du fœtus humain, Compt. rend. Soc. de biol., 1896, lxi, 33.

Ibrahim and Gross: Zur Verdauungsphysiologie des Neugeborenen, Ref. in Deutsch. med. Wehnschr., 1908, No. 25, p. 1128.

18. Ibrahim: Neuere Forschungen über die Verdauungsphysiologie des Säuglingsalters. Verhandl. d. Gesellsch. f. Kinderh., 1908, p. 25.

19. Quoted by Ibrahim (see note 18).

addition of bile,²⁰ just as it is in the adult. Ibrahim was unable to find any fat-splitting ferment in the mucous membrane of the small intestine or large intestine.

ABSORPTION

There is considerable evidence that neutral fat (unsplit fat) is not absorbed as such into the intestinal wall: for example, hydrous wool fat and paraffin, which may be made into emulsions and cannot be split, are not absorbed.²¹ It has also been shown by animal experimentation that the amount of fat in the chyme is directly proportional to the amount of fat split.²² It is also taught by some that fat is absorbed both in the form of an emulsion and in the form of water-soluble soaps, neither view excluding the other. This latter view has been strengthened by the investigations of Kastle and Loevenhart²³ who demonstrated the almost universal presence of lipase in the tissues, and showed that this ferment could reverse its action. That is to say, it can synthesize or change soaps back into neutral fats as well as split neutral fats and form soaps. It is, therefore, possible that the soaps, which have been formed during digestion, may be changed during their passage through the intestinal epithelium by the reversible action of lipase back into neutral fat, because one finds neutral fat almost exclusively in the lymph-stream. Whitehead's²⁴ experiments on cats seem to strengthen this statement, because he found that butter-fat stained with Sudan III lost the stain during absorption (soaps will not stain with Sudan III); Sudan-staining fat was seen in the lumen of the intestine; none was seen in the intestinal epithelium and a Sudan-staining fat was again found in the lacteals of the villi.

A large part of the fat absorbed goes through the portal veins to the liver,²⁵ and the rest of it is carried by the lymphatics through the thoracic duct to the blood-stream, where it may be demonstrated by the ultra-microscope. It is called digestion lipemia and commences two to three hours after meals and disappears after seven to eight hours.²⁶ The

20. Uffenheimer: *Physiologie des Magendarmkanals beim Säugling*, *Ergebn. d. inn. Med. u. Kinderh.* 1908, No. 2, 321.

21. Connstein, W.: *Arch. f. Anat. u. Physiol.*, 1899, p. 30; Henriques and Hansen: *Zentralbl. f. Physiol.*, 1900, xiv, 313.

22. Levites: *Ueber die Verdauung der Fette im tierischen Organismus*, *Ztschr. f. physiol. Chem.*, xlix, 273; liii, 349.

23. Kastle and Loevenhart: *Am. Chem. Jour.*, 1900, xxiv, 491.

24. Whitehead, R. H.: *A Note on the Absorption of Fat*, *Am. Jour. Physiol.*, 1909, xxiv, 294.

25. Weinland: *Physiologie der Leber*, *Nagel's Handb. d. Physiol.*, ii, Part 2, 456.

26. *Ueber ultramikroskopische Blutuntersuchungen zur Zeit der Fettresorption bei Gesunden und Kranken*, *Wien. klin. Wchnschr.*, 1907, p. 851; Schelble: *Untersuchungen über die Fettresorption des Säuglings*, *München. med. Wchnschr.*, 1908, No. 10; Bahrdt: *Demonstration zur Untersuchung der Lipämie beim Säugling*, *Breslauer Tagung der Freien Vereinigung für wissenschaftliche Pädiatrie*, 1908, *Monatschr. f. Kinderh.*, vii, 107.

height of the curve is dependent on the amount of fat in the food, and the age and condition of the infant.

The absorption of fat is extraordinarily good in health in babies fed on cow's milk as well as in those fed on human milk; it is usually over 90 per cent. and may be as high as 98 per cent. of the fat ingested.²⁷ Eight per cent. to 11 per cent. of the ingested fat is absorbed in the upper part of the small intestine²² and the absorption of fat is nearly complete at the ileocecal valve.²² The large intestine is capable of absorbing fat in large amounts under special favorable conditions²⁸ but under ordinary circumstances absorption here is probably very little.

Estimation of the amount of fat in the stools of babies in starvation and in health makes it probable that the greater part of the fecal fat comes from the food and not from the intestinal secretions.²⁷ It is evident, therefore, that microscopic fat that is found in the stools gives us valuable information about the digestion. It is necessary first to know how much fat may normally be found in a stool. There is a comparatively large amount of fat present in the first days of life, and this amount gradually becomes less²⁹ as the babies grow older, decreasing from 50 per cent. of the dried stools to between 14 and 25 per cent. There is so much fat passed in the stools during the early weeks that it is practically impossible to ascertain by simple microscopic examination whether there is an excess or not. In later infancy less fat is present and therefore, microscopic examinations are of more value. In normal and in many pathologic conditions the greater part of the fat, 75 per cent. or more, is split by the digestive juices and bacteria into fatty acids and soaps.

A recapitulation of the facts given above is in brief as follows: most of the fat in cows' milk or human milk is in the form of neutral fat; in normal digestion this is partially split in the stomach by the gastric lipase. When the food is emptied into the duodenum, the remainder of the fat is presumably split by the pancreatic juice and saponified by the alkalies surrounding it. This digested fat is absorbed in the small intestine between the duodenum and the ileocecal valve and only the overflow fat goes into the large intestine with the intestinal secretions and bacteria. There the fecal remains are desiccated and eventually evacuated. The normal appearance of stools varies according to the food which the infant

27. Czerny-Keller: *Der Kinder Ernährung, Ernährungsstörungen und Ernährungstherapie*, Leipzig u. Wien, 1906, p. 263; Freund: *Physiologie und Pathologie des Fettstoffwechsels im Kindesalter*, *Ergebn. d. inn. Med. u. Kinderh.*, 1909, ii, 139.

28. Hamburger, H. J.: *Ueber die Resorption von Fette und Seife im Dickdarm*, *Engelmann's Arch.*, 1900, 433.

29. Talbot, F. B.: *The Composition of Small Curds in Infants' Stools*, *Boston Med. and Surg. Jour.*, Jan. 7, 1909.

is taking. An excellent description of these stools may be found in a paper by Morse.⁵⁰

STOOLS: MICROSCOPIC EXAMINATION

Much valuable information concerning the digestion of the various food components may be obtained from careful gross and microscopic examinations of the stools. This evidence is definite and accurate and is not misleading like the symptoms obtained from mothers and nurses. There are several quick methods of estimating the fat in the stool under the microscope.

1. The first consists in staining a bit of stool with saturated alcoholic solution of Sudan III. Neutral fat drops stain red. Fatty acids may be in the form of drops or crystals; the former always stain and the latter sometimes stain. Soap splinters and crystals never stain. The total fat in the slide may be estimated by adding a drop of glacial acetic acid to the already stained preparation, and warming it gently until it begins to bubble. This changes soaps into fatty acids which are red drops as long as they remain hot and often when they become cold. The error in this method comes from the fact that it is impossible to differentiate neutral fat and fatty acid drops. I have used this stain nearly three years.

2. The second method consists³¹ in staining a scrap of stool with carbol-fuchsin and examining under the microscope. With this, neutral fat remains unstained, fatty acids stain a brilliant red and soaps a dull rose-red. Recently, I have used both stains, one on each of two cover-glass preparations, and thus obtained an estimate of the total amount of fat present, and the relative amounts of neutral fat, fatty acids, and soaps. Preparations from several parts of each stool should be examined in this way because the picture is apt to vary in stools which are not uniform.

The following terms are based on innumerable microscopic examinations of stools many of which were controlled by quantitative chemical analyses:

1. *Entire Digestion of Fat*.—Microscope, No. 7 objective, No. 3 eyepiece. Stain. alcoholic Sudan III. No fat in freshly stained specimen. One to three drops in field after acetic acid and heat.

2. *Normal Digestion*.—No fat or five to eight neutral fat-drops in the entire cover-glass in freshly stained specimen. Five to eight drops in a field after addition of acetic acid and heat. No change in amount of fecal residue.

3. *Slight Excess of Fat*.—No fat or two to four neutral fat-drops in a field. Eight to a dozen drops in a field after acetic acid and heat. No change in amount of fecal matter.

4. *Moderate Excess of Fat*.—No fat or six to eight neutral fat-drops in a field. More than twelve large drops after addition of acetic acid and heat. Considerable fecal material remains unchanged.

30. Morse, J. L.: The Stools in Infancy, New Orleans Med. and Surg. Jour., August, 1910.

31. Jacobson: Sur une réaction colorante des acides gras, Presse méd., 1906, No. 19, p. 147.

5. *Large Excess of Fat.*—No fat, or many fat-drops in a field. Practically the whole slide turns into fat-drops after acetic acid and heat, leaving very little fecal matter unchanged.

If there are any fat-drops in the original preparation it should always be stained with carbol-fuchsin to differentiate neutral fat from fatty acids. The entire cover-glass should be examined and it is usually better to examine preparations from several parts of the stool.

The following deductions can be drawn from these findings:

1. *Entire Digestion of Fat.*—It is always safe to increase the amount of fat in the food if so desired.

2. *Normal Digestion.*—It is usually safe to give more fat if necessary.

3. *Slight Excess of Fat.*—It is difficult to say how much significance should be attached to this. Probably very little.

4. *Moderate Excess of Fat.*—Without symptoms of indigestion it warns the observer to watch the fat more carefully. Yet, curiously enough, the percentage of fat may be increased without causing symptoms of indigestion and subsequently the stool may show "normal digestion." In case there are symptoms of indigestion, however, the microscope confirms our suspicions, and indicates the cause of the symptoms.

5. *Large Excess of Fat.*—This always means too much fat in the food and even if there are no symptoms, it is safer to decrease the amount of fat and examine the stool again. Usually there are symptoms of indigestion with this microscopic picture.

Fat is usually found in a normal stool in some form or other. Neutral fat appears as drops of different size and shape and sometimes as irregular flakes. When there is a very large amount it may be seen with the naked eye; it may be colorless, yellowish or slightly bile stained.

Free fatty acids may be indistinguishable from neutral fat drops except by staining with carbol-fuchsin. Neutral fat drops do not stain, while fatty acids stain; the more intense red the more acid they contain. When they are in the form of crystals, gentle warming will cause them to become drops, which recrystallize on cooling. Soaps may be amorphous or in the form of crystals. They are less shiny than fatty acids and may be stained yellow with bile coloring matter. The bushel-stained soap crystals may be in clumps and are shorter and thicker than fatty acids.

The microscopic examination of the stools of babies only occasionally gives information that the gross examination does not give, but it is a valuable control to inspection. In a few instances, the information is very surprising. It is important to bear in mind that even with considerable microscopic fat, a baby can remain perfectly happy, continue to gain and have no symptoms. This information, therefore, should be taken with reserve. In childhood, when foods other than milk are taken, small amounts of microscopic fat are of more significance. During the third year there should be only a few fat-drops on the whole slide in a normal digestion. More means a disturbance in the digestion of fat.

The closer a child comes to the adult type of diet, the more significance can be attached to information given by the microscope.

MACROSCOPIC EXAMINATION

The gross examination of the stool is the more important because it gives the most valuable information. The commonest abnormal constituents in a stool are soft, fatty curds. Soft curds are either flat white flakes (which look like undigested milk particles) or pin-head elevations; both may be present in the same stool and they are always associated with more or less mucus, which is stained green or yellow. About 60 per cent. of their dried substance is fat. These curds are usually present at one time or other in the stools of all nursing babies and are of no significance even with slight symptoms of indigestion. They are more important in the stools of bottle-fed babies. If there are no symptoms of indigestion and the baby is gaining and happy, the percentage of fat should not be changed, but the significance of these curds should be remembered. If there are symptoms of indigestion, loss of weight, and soft, fatty curds in the stools, there is too much fat in the food. When it is diminished, the curds disappear, the baby becomes happy and gains weight.³²

These curds should not be confused with tough casein curds, which are white or bile-stained, bean-like masses of varying size and shape. They may be easily differentiated from the fat curd by their physical characteristics. The latter will smooth out on a napkin while the former will not; casein hardens in liquor formaldehydi (formalin) while fat does not. I recently proved³² by the precipitin reaction that the protein in these curds is cow-casein. They contain varying amounts of neutral fat which is entangled in the meshes of the casein when it coagulates in the stomach. This fat has not been acted on by the digestive juices because it is protected by a coating of casein. It is present in larger or smaller amounts, according to the percentage of fat in the milk and may, therefore, be considered accidental.³³

Soap stools are very light yellow or white, usually smooth, sometimes salve-like, at other times dry and brittle. The shiny appearance of the fresh surface suggests fat. They are composed almost entirely of soap. Fifty per cent. to 70 per cent. of their dried substance may be fat. They often occur in constipation due to too much fat in the food and disappear when the fat is replaced by other food components. They may be the precursors of a fat diarrhea and if their full significance is not appreciated, they may eventually become part of the clinical picture of infantile atrophy.

32. Talbot, F. B.: Casein Curds in Infants' Stools. Biological Proof of Their Casein Origin, *Arch. Pediat.*, June, 1910.

33. Talbot: The Composition of Large Curds in Infants' Stools, *Boston Med. and Surg. Jour.*, June 11, 1908.

Fat stools are very bright yellow (like Indian meal), oily and soft. They are composed of large amounts of fats, a good proportion of which is in the form of neutral fat or fatty acid. When one of these stools is placed on paper and then removed, there remains behind a grease-spot which will not absorb water (oiled paper). They are usually accompanied by very severe symptoms. Fat should be removed entirely from the milk for a time and very frequently these babies cannot be saved without human milk.

METABOLISM

Most of the figures offered us by metabolism experiments are obtained by the Rosenfeld method of extracting fat, and very recently by the Kumagawa and Suto method. These and other modern methods of fat extraction have been given in more or less detail in the appendix of this paper. Despite the fact that the figures so obtained may not be absolutely correct, I believe that they are of great relative value and help to clear up many of the cases of perverted digestion. While they do not say the final word on the subject, they lead to a more intelligent grasp of the pathology of digestion. This paper does not pretend to consider the rôle of the intestinal flora in normal and abnormal digestion, but I believe that they are of great significance in certain conditions and that they will be found to influence metabolism. For example, Kendall³⁴ has shown that two factors are necessary for fermentation: a carbohydrate food, and fermentative bacteria; in like manner putrefaction cannot take place without protein plus putrefactive bacteria. Fermentative bacteria cannot act on protein, and putrefactive bacteria cannot act on carbohydrate. It is very difficult, therefore, to draw any conclusions in a subject which is complicated by so many factors. The problems of digestion depend on the balance of all the factors concerned and when the normal balance is upset by any one or many factors, we have a pathologic condition.

The significance of fatty acids and soaps is as yet unknown; probably they are of very little significance in the questions of absorption. Freund (quoted above) has shown that an acid dyspeptic stool can be changed in many instances to a formed "soap stool" by a relative increase in the amount of casein, while an alkaline soap stool can be changed into an acid stool by a relative increase in the amount of carbohydrates. Coincident with the change from an acid to an alkaline stool (according to Kendall) there is a change of the intestinal flora; the acid-forming bacteria which previously predominated are replaced by the putrefactive group of bacteria. When an alkaline stool is made acid the reverse takes

34. Kendall: Boston Med. and Surg. Jour., 1911, clxiv (to appear in March). Read before Suffolk District Medical Society.

place. Bahrđt³⁵ has recently shown that babies passing "soap stools" have diminished powers of absorption and that they lose more fat than was formerly taught. He found the absorption of fat (Kumagawa and Suto method) as follows:

Name of Baby.	Age, Months.	Weight, Gm.	Fat ab- sorbed. Per cent.	Character of Stools.
Schröder, 7 days	9	7470	82.4	Soap stools
Schüler, 7 days	2	3945	83.2	Mostly soap stools
Weiss, Ia, 5 days....	9/10	3750	81.9	Soap stool
Weiss, Ib	9/10	3750	86.0	Soap stool
Weiss II, 8 days.....	10	3900	93.0	Normal stools
Breast and skim milk.				

The fat absorption in these babies with soap stools is, therefore, considerably less than that of normal infants. There is, however, not such a loss of fat as in diarrhea. There is a loss of magnesium and calcium³⁶ in these soap stools and there is no loss of sodium and potassium. If the stools become acid and change into soft fatty curds there is no longer a loss of calcium and magnesium, but there is a loss of sodium and potassium. With this change comes an increased loss of fat from the body.³⁸ If this condition becomes more pronounced with diarrhea, there is a considerable loss of fat with the alkalies; the baby loses weight and takes on the appearance of "infantile atrophy."³⁷ Such babies can only be saved by human milk.³⁸

Biedert³⁹ and Demme⁴⁰ designated severe chronic disturbances of digestion in which the stools contained very large amounts of fat as "fat diarrhea." The latter had one such case which came to autopsy and was found to have disease of the pancreas. Hecht⁴¹ and Reuss⁴² have reported cases of congenital obliteration of the bile-duct with normal pancreas, in which only one-half of the fat was split. I examined the stools

35. Bahrđt, H.: Untersuchungen über das Symptom der Seifenbildung und die Ausscheidung der Basen im Darm des Säuglings, *Jahrb. f. Kinderh.*, 1910, lxxi, 249.

36. Meyer, L. F.: *Jahrb. f. Kinderh.*, April, 1910, p. 379.

37. Finkelstein: Ueber Alimentäre Intoxikation III, *Jahrb. f. Kinderh.*, 1908, lxxviii, 521 and 692.

38. Finkelstein's so-called alimentary intoxication will not be considered in this paper because I believe that the majority of cases which clinically come under this category are not diseases of metabolism, but are bacterial infections of the gastro-intestinal canal, and that the physiologic powers of digestion are so lowered by the disease that the various food components are not digested.

39. Biedert: *Jahrb. f. Kinderh.*, 1879, xiv, 336; *ibid.* 1888, xxviii, p. 21.

40. Demme: *Jahrb. über die Tätigkeit des Jammerschen Kinderspitals in Berlin*, 1874 and 1877; quoted from Hecht, *Die Faeces des Säuglings*, etc., p. 128.

41. Hecht: *Die Faeces des Säuglings und Kindes*, Berlin-Wien, 1910, p. 128.

42. Reuss: Case of Obliterated Bile Duct (congenital) Reported in Discussion, *Jahrb. f. Kinderh.*, December, 1908, 729.

of a baby, the autopsy on which showed biliary cirrhosis⁴³ and a patent bile-duct, and found a similar type of stool.

Tuberculous peritonitis in babies is primarily a disease of the lymphatic system and when the mesenteric glands become caseous they form a dam beyond which the fat cannot pass. It has been shown earlier in this paper that part of the fat is normally carried by the lymphatics to the blood stream. If this road is blocked with tuberculous tissue, it is reasonable that some of the fat should be lost from the body. I have found large amounts of fat in the stools of such babies. Hecht believes that 80 per cent. of the fat in the stool should be split, and considers that great divergence from this amount means either trouble with the bile or pancreatic juice. He reports a seven months, premature baby which was only able to split 53 per cent. of the fat, and considers this to be due to weak action of the pancreatic fat-splitting enzyme, which presumably is not completely developed. Finizio⁴⁴ explains a large amount of fat in the stool of an 11-months-old baby with mumps by probable trouble in the pancreas.

Czerny⁴⁵ believes that babies with an exudative diathesis can be harmed by fat. He finds that an increase in the amount of fat in the food will bring eruptions out on the skin. Steinitz and Weigert⁴⁶ have apparently proved the correctness of this assumption by a metabolism experiment.

There is no doubt that large amounts of fat can do a great deal of harm to most babies. Such babies come under two classes—those which have a normal digestion and are unable to digest excessive amounts of fat, and those which have diminished powers of digestion and are unable to digest normal amounts of fat. So much attention has been paid to the few babies that are unable to digest fat that we are apt to forget that most babies can digest fat within reasonable limits. L. F. Meyer⁴⁷ has recently shown in Finkelstein's clinic that when fat is increased in the food of normal healthy babies there is no loss of fat, or salts from the body. This dispels, in a very convincing way, the false impression that normal babies are unable to digest fat. John Howland of New York showed in a recent investigation (not yet published) that a baby could be fed on large quantities of fat without symptoms of indigestion and without acidosis. In my experience, it has been safe to increase the

43. Morse, J. L.: Jaundice in the New-Born, Boston Med. and Surg. Jour., Feb. 24, 1910.

44. Finizio: A Case of Fat Diarrhea Following Mumps, *Pediat.*, September, 1909; Rev. in *Jahrb. f. Kinderh.*, 1910, lxxi, 205.

45. Czerny: Zur Kenntnis der exudative Diathese, Part 1, *Monatschr. f. Kinderh.*, 1906, iv, 1; *ibid.* Part 2, 1908, vi, 1; *ibid.* Part 3, 1909, vii, 1.

46. Steinitz and Weigert: *Monatsch. f. Kinderh.*, 1910, ix, 385.

47. Meyer, L. F.: *Jahrb. f. Kinderh.*, April, 1910, p. 379.

percentage of fat gradually up to 4 per cent. in most normal babies whose digestive powers have not previously been lowered by gross errors in feeding or by infection, and that they develop normally without any of the signs or symptoms of fat indigestion so long as their hygiene is perfect and they have no intercurrent infection.

APPENDIX

METHODS OF ESTIMATION OF FAT IN FECES

There is no such thing as a theoretically perfect method of estimating fat in the feces. The methods employed may be grouped under two heads: 1. Extraction methods which attempt to obtain all the substances soluble in ether. 2. Saponification methods, in which the higher fatty acids are set free by saponification from the various combinations in which they occur, separated as far as possible from the other products of the action of alkali used, and weighed as fatty acids.

EXTRACTION METHODS

These methods estimate all the substances soluble in ether without considering what form the fat was in. The criterion in determining the value of the particular method under consideration has been the gross yield of substance soluble in ether. The method which has been taken as a standard in recent years is that of Rosenfeld, because it gave higher yields than other methods of substances soluble in ether. This method has been criticized because the substances weighed contain nitrogen and phosphorus and a low percentage of fatty acid. I used a modification of this method⁴⁸ as follows:

The feces are weighed, thoroughly mixed with 95 per cent. alcohol and dried at 43-45 C., transferred to a desiccator, and dried to constant weight. A weighed portion of the dried feces is placed in a paper capsule and boiled in absolute alcohol for one-half hour. The capsule is then transferred to a Soxhlet tube and extracted eighteen hours with chloroform. The combined absolute alcohol and chloroform extracts are evaporated to dryness, and the residue from each extracted with petroleum ether. The petroleum ether is then filtered and the filter paper thoroughly washed with warm petroleum ether until the wash ether shows no trace of fat, by evaporation on a watch glass. The filtrate is evaporated to constant weight. This weight is recorded as representing the quantity of neutral fat and fatty acid in the weighed portion of dry stool.

The dishes used for the evaporation of the alcohol and chloroform extracts from the first extraction are washed with hot 3 per cent. hydrochloric acid alcohol. The filter paper, used for filtering the petroleum ether in the first step, is added to the capsule from which the neutral fat and fatty acid have been extracted and boiled one-half hour under a reflux condenser in 3 per cent. hydrochloric alcohol to which the HCl alcohol washings from the dishes, mentioned in the first step, are added. Next, it is boiled one-half hour with absolute alcohol: the combined capsule and filter paper are then transferred to a Soxhlet tube and extracted for eighteen hours. The hydrochloric acid absolute alcohol and chloroform extracts are evaporated separately, the residue in each is taken up in petroleum ether and the combined petroleum ether extract is filtered. The filtrate is evaporated to constant weight; this represents soaps.

The neutral fat and fatty acids (the fat first weighed) are dissolved in equal parts of absolute alcohol and sulphuric ether and the acidity determined by titrating against decinormal alcoholic sodium hydrate solution, using phenolphthalein as an indicator.

Kumagawa and Suto⁴⁹ found that the solvent which gave the largest yield of substances soluble in ether was alcohol used near its boiling point in a continu-

48. Boston Med. and Surg. Jour., Jan. 11, 1908.

49. Kumagawa and Suto: Ein neues Verfahren zur quantitativen Bestimmung des Fettes und der unverseifbaren Substanzen im tierischen Material nebst der Kritik einiger gebräuchlichen Methoden, I, Biochem. Ztschr. 1908, viii, 212.

ous extraction apparatus. This explains why the Rosenfeld method and its modifications obtain higher yields of fat than other methods. The Rosenfeld method, however, is the best one yet devised to estimate the relative proportion of neutral fat, fatty acids and soaps.

Folin and Wentworth⁵⁰ criticize this method because they have observed that prolonged chloroform extraction brings away materials with a distinct fecal odor, and they say that the best method for extraction is that which takes out the smallest amount and not that which extracts the largest amount. They have devised a method which apparently has many advantages over the Rosenfeld method. It is briefly as follows:

One gram of very finely powdered feces is weighed into a fat-free paper capsule, placed in an extraction apparatus and boiled twenty hours with an ethereal hydrochloric acid solution. The ether is then distilled off and with it goes the hydrochloric acid. A low boiling petroleum ether (Ligroin) is added and allowed to stand over night. This solution is filtered the next day into a weighed beaker and dried at a temperature of 95 C. for five hours. It is then dried and weighed as neutral fat and fatty acids. The next step is a new departure in chemistry, according to Folin and Wentworth, and is very important. The fat is dissolved in benzol, .5 per cent. alcoholic phenolphthalein added and it is heated almost to boiling. It is then immediately titrated against N/10 sodium alcoholate (made by dissolving 2.3 gm. metallic sodium in one liter absolute alcohol and standardized); 1 c.c. of this=28.4 m.gm. stearic acid. This method of titration undoubtedly has a great advantage over all that have been devised thus far.

SAPONIFICATION METHOD

Lieberman-Szekely described a method of determining the fat in the stool by first saponifying it and then splitting with acid and extracting with ether. This extract was purified with petroleum ether. This method does not estimate the fat in the stool, but all the higher non-volatile fatty acids in various combinations; and according to Kumagawa-Suto the fat may be reckoned from this by multiplying by the factor 1.046.

Kumagawa and Suto's⁴⁹ method gives the highest results of all methods and has been controlled by very accurate and painstaking experiments. It is as follows:

Two to 5 gm. of powdered feces are mixed in a beaker with 25 c.c. 5 per cent. NaOH (20NaOH in 100 c.c.) and heated two hours over a water bath. The beaker should be covered with a watch glass during this process. During the saponification the mixture is stirred now and then with a glass rod. After about ten minutes the powder dissolves and there are small flocculi left behind. After about two hours, the solution is transferred, still hot, into a hermetically closed separating funnel with a capacity of 250 c.c. The beaker is washed two or three times with about 5 c.c. warm water. Next the solution is acidified with 30 c.c. 20 per cent. H₂SO₄. After cooling well 70 to 100 c.c. ether is added and shaken well. A precipitate remains between the layers of solution. The clear water is decanted after separation. Then the brown colored ether is carefully decanted into a beaker. The funnel with the precipitate is washed twice with ether; it is then dissolved and shaken again with 30 to 50 c.c. ether and to that is added the strongly acid water of the first shaking, and it is again well shaken. The reaction is then acid and the remaining fatty acid is dissolved in the ether. These ether extracts are united, evaporated and again taken up with absolute ether, filtered through asbestos and evaporated. This extract, which contains coloring matter, fatty acid, lactic acid and other components, is heated at 50 C. first and extracted with petroleum ether. If this solution is milky it is allowed to stand one hour and then filtered through asbestos, dried at 50 C. and weighed. More detail concerning this method may be obtained by referring to Kumagawa and Suto's original article in which there is a vast amount of experimental data and criticism of other methods. In it the bibliography concerning the extraction of

50. Folin and Wentworth: Determination of Fat and Fatty Acid, Jour. Biol. Chem., June, 1910.

fat from the animal tissue is very complete. These findings have been substantiated by Inaba.⁵¹

Bahrdrf, Edelstein, Langstein and Welde⁵² have used a new method for the quantitative estimation of the free volatile fatty acids in the feces. This method is based on a method by W. Steinkef which used vacuum distillation and steam for extraction. The method in brief is as follows:

A weighed amount of fresh feces was distilled in a temperature of 60 C. for two hours, with steam drawn through on the one side by a vacuum on the other. The distillate is titrated against N/10 sodium hydrate, with phenolphthalein as an indicator. The amount of acid present is estimated in terms of decinormal acid. The temperature of the water bath during the whole distillation should be 60 C. Generally the distillation goes well if there are 600 to 900 c.c. distillate in one hour. The original article should be consulted for detail of the method and the apparatus necessary.

This brief description of the newer methods of fat and fatty acid extraction has been added so that those who have a desire to commence metabolism work on babies will be able to choose for themselves and go back to the original sources. I feel that the last word has not been said, and that it is necessary to extract all feces, both by the Kumagawa and Suto method, and by some modification of the Rosenfeld method. The method offered by Folin and Wentworth is still in the experimental stage and the writers are "now working to perfect it."

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BIBLIOGRAPHY

The following additional references cover as many of the important works on this subject as possible, without making it unwieldy. An attempt has been made to give only those references which are up to date and have stood the test of time.

Abderhalden, E., and Brahm, D.: Ist das am Aufbau der Körperzellen beteiligte Fett in seiner Zusammensetzung von der Art des aufgenommenen Nahrungsfettes abhängig? *Ztschr. f. physiol. Chem. Strass.*, 1910, lxxv, 330.

Adler, Max: Contributions to the Question of Fat Absorption under Pathological Conditions in Men and Animals, *Ztschr. f. klin. Med.*, 66, p. 302.

Amberg, S., and Morrill, P.: A Study of the Metabolism of a Breast-fed Infant with Special Reference to the Ammonia Co-efficient. *Proc. Am. Soc. Biol. Chem.*, 1908, p. 35.

Ballantyne: Quoted by Savonnat, *Arch. de Méd. des Enf.*, 1906, xi, No. 1.

Bendix: Ein Stoffwechselversuch beim atrophischen Säugling, *Engelmann's Arch.*, 1899 (Suppl.), p. 206.

von Bergmann, S., and Reicher, K.: Zur Pary'schen Hypothese der Fettbildung in der Darmwand, *Ztschr. f. exp. Path. u. Therap., Berl.*, 1908-1909, v, 742.

Biedert: Kinderernährung im Säuglingsalter, ed. 4, Stuttgart, 1900.

Biernatzki: Ueber den Einfluss der überfetteten Nahrung auf den Magendarmkanal und den Stoffwechsel, *Zentralbl. f. Physiol. u. Path.*, 1907, N. F. 2, p. 401.

Birk: Ueber den Magnesiumumsatz des Säuglings, *Jahr. f. Kinderh.*, 1907, lxxvi, 300; Untersuchungen über den Einfluss des Phosphorlebertrans auf den Mineralstoffwechsel gesunder und rachitischer Säuglinge, *Monatschr. f. Kinderh.*, 1908, vii, 450.

Blauberger: Experimentelle und kritische Studien über Säuglings feces, Berlin, Hirschwald, 1897.

Boldyreff: Ueber den selbständigen und künstlich hervorgerufenen Uebergang von Pancreassaft in den Magen und über die Bedeutung dieser Erscheinung für die praktische Medizin, *Zentralbl. f. Physiol. u. Path.*, 1908, N. F. 3, p. 209.

Budin: *The Nursling*, Caxton Pub. Co., London, 1907.

51. Inaba: *Biochem. Ztschr.*, 1908, viii, 352.

52. Bahrdrf, Edelstein, Langstein and Welde: Untersuchung über die Pathogenese der Verdauungsstörungen im Säuglingsalter, *Ztschr. f. Kinderh.*, 1910, i, No. 2, 139.

Camerer, Sen.: Das Energiegesetz in der Menschlichen Physiologie, Jahrb. f. Kinderh., 1907, lxvi, 129.

Camerer, jun.: Untersuchung über die Ausscheidung des MilCHFettes, Verhandl. d. Gesellsch. f. Kinderh., 1906, p. 135.

Camus, J., and Nieloux: Contribution à l'étude de la digestion des graisses dans les différentes segments du tube digestif, Compt. rend. Soc. de biol., 1910, lxxviii, 619; Abstr. in Chem. Abstracts, 1910, iv, No. 17; Digestion intra-gastrique des graisses sans l'influence de la lipaséine. Compt. rend. Soc. de biol., 1910, lxxviii, 680.

Chacuet: Recherches sur l'absorption des graisses, etc., Thèse de Paris.

Cohnheim: Physiologie der Verdauung, in Nagel's Handb. d. Physiol., ii, 516.

Cohnheim, O., and Dreyfuss, S. L.: Zur Physiologie und Pathologie der Magenverdauung, Ztschr. f. physiol. Chem., 1908, lviii, 50.

Connstein: Ueber fermentative Fettsplaltung. Asher-Spiro, Ergebn. d. Physiol., 1904, i, 194.

Croner, W.: Versuche über Resorption von Fetten im Dünndarm, Biochem. Ztschr., 1910, xxiii, 97.

Czerny: Ueber die Beziehungen zwischen Mästung und skrofulösen Hautaffektionen, Monatschr. f. Kinderh., 1904, ii, 57; Die Exudative Diathese, Jahrb. f. Kinderh., 1905, lxi, 198.

Dormeyer, C.: Die quantitative Bestimmung von Fetten, seifen und Fettsäuren in thierischen Organen, Pflüger's Arch., 1897, lxxv, 90.

Emmett: The Determination of Fatty Matter in Normal Feces by Ether and Carbon. Tetrachlorid. Jour. Am. Chem. Soc., June, 1909, p. 693.

Engel: Ueber das Fett der Frauenmilch, Ztschr. f. phys. Chem., 1905, xlv, 354; Zur Secretions physiologie des MilCHFettes, Med. Klinik, 1905, No. 24.

Engel: Nahrungsfett und MilCHFett. Verhandl. d. Gesellsch. f. Kinderh. in Meran, 1906, No. 22.

Engel: Zur Kenntnis der Magensaftsekretion beim Säugling, Arch. f. Kinderh., 1908, xlix, 16.

Engel and Plauth: Art und Menge des Fettes in der Nahrung Stillender Frauen und die Wirkung seiner Entziehung auf das MilCHFett, München. med. Wehnschr., 1906, p. 1158.

Faust and Talquist: Ueber die Ursachen der Bothryocephalusanämie, Schmiedeberg's Arch., 1907, lvii, 380.

Faust and Schmincke: Ueber chronische ölsäurevergiftung, Schmiedeberg's Arch., 1908, p. 171; Festschrift für Schmiedeberg.

Finizio, S.: Sulla digestione gastrica dei grassi nel lattante. Pediat., Napoli, 1910, q. s., viii, 1-24; Rev. in Jahrb. f. Kinderh., April, 1910, 503.

Finkelstein: Zur diätetischen Behandlung des konstitutionellen Säuglings-ekzems, Med. Klinik, 1907, 1098.

Frank: Zur Lehre von der Fettresorption, Ztschr. f. Biol., 1898, xxxvi, 568.

Freund, W.: Bemerkungen zu der Arbeit von P. Reyler über den Fettgehalt der Frauenmilch. Jahrb. f. Kinderh., 1905, lxi, 900; Zur Wirkung der Fettdarreichung auf den Säuglingsstoffwechsel, Jahrb. f. Kinderh., 1905, N.F., lxi, 36; Milchnährschaden und Fettresorption. Vortrag auf der Dresdner Tagung der freien Vereinigung für wissenschaftliche Pädiatrie, Ref. Monatssch. f. Kinderh., 1908, vi, 54; Säuren und Basen im Urin kranker Säuglinge. Monatschr. f. Kinderh., 1903, i, 230; Zur Kenntnis des Fet und Kalkstoffwechsels im Säuglingsalter, Biochem. Ztschr., 1909, xvi, 453.

Friedenthal: Ueber die Permeabilität der Darmwandung, etc., Engelmann's Arch., 1902, 149 and Supp., 449.

Gilkin, W.: Untersuchungen zur Methode der Fettbestimmung im thierischen Material, Pflüger's Arch., 1903, xcv, 107.

Gillet: Le trouble de la sécrétion pankreatique chez les enfants. Quoted by Czerny-Steinitz in Von Noorden's Handbook, Pathology of Metabolism, iii, 833. W. T. Keener & Co., Chicago, 1909.

Glaessner and Singer: The Liver in Respect to Absorption of Fat, *Med. Klin.*, 1909, No. 51, 1917.

Grosser: Der Chemismus bei Pylorusstenose, *Monatschr. f. Kinderh.*, vii, 106.

Hall, Walker: Examination of Fat in Feces, *Canadian Pract. and Rev.*, March, 1908.

Hamburger, H. J.: Sind es ausschliesslich die Chylusgefässe welche die Fettresorption besorgen, *Engelmann's Arch.*, 1900, 554.

Hamsik, A.: Reversible Wirkung der Darmlipase, *Ztschr. f. physiol. Chem.*, 1909, ix, 1.

Hartley, P.: On the Nature of Fat Contained in the Liver, Kidney and Heart, *Jour. Physiol.*, 1907, xxxvi, 17; *Jour. Physiol.*, 1909, xxxviii, 353.

Hartley and Mavrogordato: Fat in Normal and Pathological Livers, *Jour. Path. Bact.*, 1908, xii, 371.

Hecht: Ueber das Verhalten der Eiweiss und Fett Spaltenden Fermente im Säuglingsalter. *Wien. klin. Wehnschr.*, 1908, 1551; Untersuchungen über die Fettresorption auf Grund der chemischen Zusammensetzung der Fette, *Jahrb. f. Kinderh.*, 1905, lxii, 612; Vorschlag einer klinischen Prüfung der Fettresorption, *Wien. klin. Wehnschr.*, 1907, No. 17: Ueber die Bedeutung der Seifenstühle im Säuglingsalter. *München. med. Wehnschr.*, 1908, 1010; Das Verhalten der Fettsäurebildung im Darminhalt des Säuglings, *München. med. Wehnschr.*, 1910, lvii, 62.

Heinsheimer: Experimentelle Untersuchungen über fermentative fettspaltung im Magen. *Deutsche med. Wehnschr.*, 1906, p. 1194.

Heubner and Rubner: Die natürliche Ernährung eines Säuglings, *Ztschr. f. Biol.*, 1898, xxxvi, p. 1; Die künstliche Ernährung eines normalen und eines atrophischen Säuglings, *Ztschr. f. Biol.*, 1899, xxxviii, p. 315.

Hoffmann, E.: Ueber mikroskopische Fäcesuntersuchungen, *Monatschr. f. Kinderh.*, 1907, vi, p. 662; Fermentuntersuchungen und Fettresorption beim Säugling, *Jahrb. f. Kinderh.*, 1910, xxii, 280.

Howland: Fat Incapacity in Infants and Children, *Arch. Pediat.*, 1908, xxv, 225.

Hüssy: Zur Kenntniss der Acidosis im Kindesalter, *Zentralbl. f. d. ges. Physiol. u. Path. d. Stoffwechsels*, N. F., 1906, p. 1.

Ibrahim, J.: Zur Verdauungsphysiologie des menschlichen Neugeborenen, *Ztschr. f. physiol. Chem.*, 1910, lxiv, 95.

Jakobson, G.: Graisses neutres et acides gras dans les selles des nourissons, *Compt. rend. Soc. de biol.*, 1909, lxxvii, 145.

Jäckle: Ueber die Zusammensetzung der menschlichen Fette, *Ztschr. f. physiol. Chem.*, 1902, xxxvi, 52.

Joannovics and Pick: Rôle of the Liver in Resorption of Fat, *Wien. klin. Wehnschr.*, xxiii, 673.

Johannessen and Wang: Studien über die Ernährungsphysiologie des Säuglings, *Ztschr. f. physiol. Chem.*, 1898, xxiv, 482.

Loevenhart: On the Relation of Lipase to Fat Metabolism Lipogenesis, *Am. Jour. Phys.*, 1902, vi, 331.

Keller: Phosphor und Stickstoff im Säuglingsorganismus, *Arch. f. Kinderh.*, 1900, xxix, 1; Fettumsatz und Acidose, *Monatschr. f. Kinderh.*, 1903, i, 234; Zur Kenntnis der Gastroenteritis im Säuglingsalter, II Mitt. Amnionakauscheidung, *Jahrb. f. Kinderh.*, N. F., xlv, 25.

Knöpfelmacher: Untersuchungen über das Fett im Säuglingsalter und über das Fettsklerem, *Wien. klin. Wehnschr.*, 1897, 228; Die Ausscheidung flüssiger Fette die Faeces und die Resorption des Milchfettes bei Kindern, *Wien. klin. Wehnschr.*, 1897, 695.

Knöpfelmacher and Lehdorf: Das Hautfett im Säuglingsalter, *Ztschr. f. Exper. Path. u. Therap.*, 1906, ii, 133.

Krause, P.: Lipämie im Coma diabeticum, *Verhandl. d. Kongresses f. inn. Med.*, München, 1906, xxiii, 521.

Lange and Berend: Stoffwechselversuche an dyspeptischen Säuglingen, *Jahrb. f. Kinderh.*, 1897, xlv, 339.

Langstein and Lempp: Die Bedeutung des Fettes für die Verdauung der Milcheiweisskörper, *Monatsch. f. Kinderh.*, 1907-8, vi, 55.

Langstein and Meyer: Die Acidose im Kindesalter, Part I, *Jahrb. f. Kinderh.*, 1905, lxi, 454; Part II, *Jahrb. f. Kinderh.*, 1906, lxiii, 30; Säuglingsernährung und Säuglingsstoffwechsel, Ein Grundriss für den praktischen Arzt, Wiesbaden, 1910.

Langstein and Steinitz: Zucker und Lactaseausscheidung beim magendarmkranken Säugling, *Hofm. Beitr.*, 1905, vii, 575.

Langstein and Niemann: Ein Beitrag zur Kenntniss der Stoffwechselvorgänge in den ersten vierzehn Lebenstagen normaler und frühgeborener Säuglinge, *Jahrb. f. Kinderh.*, 1910, lxxi, 604.

Laves: Untersuchung des Fettes der Frauenmilch, *Ztschr. f. physiol. Chem.*, 1894, xix, 369.

Leathes, J. B.: Functions of the Liver in Relation to Metabolism of Fats, *Lancet*, London, 1909, clxxvi, 594.

Leathes and Wedell: Desaturation of Fatty Acids in the Liver, *Jour. of Physiol.*, 1909, 38 Proc., xxxviii and xl.

Lehndorf: Ueber das Magenfellpolster der Säuglinge, *Jahrb. f. Kinderh.*, 1907, lxvi, 286.

Lewinsky: Die gewinnung des Pankreassekretes aus dem Magen und ihre diagnostische Verwertbarkeit, *Deutsch. med. Wehnschr.*, 1908, 1582.

Liebermann and Székely: Eine neue Methode der Fettbestimmung in Futtermitteln, Fleisch, Koth, etc., *Pflüger's Arch.*, 1898, lxxii, 360.

Litmanowicz and Müller: Ueber das Verhalten des Ptyalins unter normalen und krankhaften Bedingungen, *Zentralbl. f. d. gesamte Phys. u. Path. d. Stoffwechsels*, 1909, No. 3.

London: Zum Chemismus der Verdauung im tierischen Körper VII Mitteil. Ein reiner Pylorusfistelhund und die Frage über gastrolipase, *Ztschr. f. physiol. Chem.*, 1906-1907, 1, 125; *ibid.* 1909, lx, 191; Zum Studium der allmählichen Fortbewegung Verdauung und Resorption der Eiweisstoffe, Fette, und Kohlenhydrate bei einzelner Darreichung und bei der Darreichung in verschiedenen Kombinationen, *Ztschr. f. physiol. Chem.*, 1909, lx, 194.

Magnus-Levy: Die Acetonkörper. *Argebn. d. inn. Med. und Kinderh.*, 1908, i, 352.

Meyer, L. F.: Beitrag zur Kenntniss der Unterschiede zwischen natürlicher und künstlicher Ernährung, *Verhand. d. Gesellsch. f. Kinderh.*, 1906, 122; Zur Kenntniss des Mineralstoffwechsels im Säuglingsalter, *Biochem. Ztschr.*, 1908, xii, 422; Zur Kenntniss des Stoffwechsels bei der alimentären Intoxikation, *Jahrb. f. Kinderh.*, 1907, lxv, 585; Zur Kenntniss der Acetonurie bei den Infektionskrankheiten der Kinder, *Jahrb. f. Kinderh.*, 1905, lxi, 438; Salzstoffwechsel beim normalen und ekzematösen Säugling, *Monatsch. f. Kinderh.*, 1908-9, vii, 104; Die Bedeutung der Mineralsalze bei den Ernährungs Störungen des Säuglings, *Jahrb. f. Kinderh.*, 1910, lxxi, 1.

Moll: Fat Content of the Mucus Membrane of the Small Intestine During Absorption of Fat, *Zentralbl. f. Physiol.*, 1909, xxiii, 290.

Monges, J.: Soap in Feces, *Compt. rend. soc. de biol.*, 1909, lxvii, 596.

Mottram, V. H.: Fatty Infiltration of the Liver in Hunger, *Jour. Physiol.*, 1909, xxxviii, 281; A Method of Fatty Acid Extraction, *Jour. Physiol.*, 1910, xl, 122.

Müller, Erich: Beitrag zur Frage der natürlichen Nutztstoffe der Frauenmilch, *Berl. klin. Wehnschr.*, 1908, No. 22.

Munk, I.: Ueber Darmresorption nach Beobachtungen an einer Lymphfistel Menschen, *Arch. Anat. Physiol. (Physiol. Abth.)*, 1890, 376; Zur Lehre von der Spaltung und Resorption der Fette, *Arch. Anat. Physiol. (Physiol. Abth.)*, 1890, 581.

Neumann, Julius: Ueber Beeinflussung der tryptischen Verdauung durch Fettstoffe, Berl. klin. Wehnschr., 1908, No. 46, 2066.

Neisser and Bräuning: Ueber Verdauungslipämie, Ztschr. f. exp. Path. u. Therap., 1907, iv, 747.

Neumann, J.: Zur Theorie der Schädigung magendarmkranker Säuglinge durch fetthaltige Ernährung, Arch. f. Kinderh., 1909, I, 45; Ueber Beeinflussung der tryptischen Verdauung durch Fettstoffe; Berl. klin. Wehnschr., 1908, xlv, 2066.

Noll, A.: Ueber Fettsynthese im Darmepithel des Frosches bei der Fettresorption, Arch. f. Physiol., 1908, Suppl., 145.

Von Noorden: Handbook of Pathology of Metabolism, Eng. Ed. published by W. T. Keener & Co., Chicago, 1907.

Oppel, A.: Lehrbuch der vergleichenden mikroskopischen Anatomie, 1897, ii; Verdauungs-Apparat, Ergebn. d. Anat. u. d. Entwickl., 1902, xii, 61.

Orgler: Der Eiweissstoffwechsel des Säuglings, Ergebn. der inn. Med. u. Kinderh., 1908, ii, 464; Beiträge zur Lehre von Stickstoffwechsel im Säuglingsalter, Monatschr. f. Kinderh., 1908, x, 135; Ueber Entfettungskuren im Kindesalter, Jahrb. f. Kinderh., 1905, lxi, 106.

Overton: Ueber den Mechanismus der Resorption und Sekretion, Nagel's Handbuch der Physiol. II, 890.

Pflüger: Die Resorption der Fette vollzieht sich dadurch, das sie in wässrige Lösung gebracht werden, Pflüger's Arch., lxxxvi, 1.

Phillips, F.: Dextrinisiertes und nicht dextrinisiertes Mehl in der Säuglingsnahrung, Monatschr. f. Kinderh., 6, 1908, vi, 26.

Plant, O. H.: Absorption of Fat from an Isolated Loop of Small Intestine in Healthy Dogs, Am. Jour. Physiol., 1908, xxiii, 65.

Raczynski: Die saure Dyspepsie der Brustkinder, Przegląd lekarski, 1902, Nos. 26-29; Ref. in Monatschr. f. Kinderh., 1903, i, 30; Dyspepsia Intestinalis Acida Laetorum, Wien. klin. Wehnschr., 1903, 342.

Radnitz: Sammelreferat über die Arbeiten aus der Milchchemie, Monatschr. f. Kinderh., 1903-4, ii, 422; *ibid.* 1905-6, iv, 258.

Reyber: Ueber den Fettgehalt der Frauenmilch, Jahrb. f. Kinderh., 1905, lxi, 601; Beitrag zur Frage nach dem Nahrungs- und Energiebedürfniss des natürlich ernährten Säuglings, Jahrb. f. Kinderh., 1905, lxi, 553.

Rietschel: Ueber die Lipase im Magensaft des Säugenden Tieres, Monatschr. f. Kinderh., 1907-8, vi, 333.

Rosenberg: Zur Physiologie der Fettverdauung, Arch. f. Physiol., 1901, lxxxv, 152.

Rosenfelt: Zu den Grundlagen der Entfettungsmethoden, Berl. klin. Wehnschr., 1899, 665; Fettbildung bei Asher-Spiro, Ergebn. d. Physiol. 1902, ii, I Abteil., 651; Fettbildung bei Asher-Spiro, Ergebn. d. Physiol., 1903, iii, 50 Abteil.; Zur Methodik der Fettbestimmung, Centr. f. Inn. Med., 1900, xxi, 833.

Rothberg: Ueber den Einfluss organischer Nahrungskomponenten (Eiweiss, Fett, Kohlehydrate) auf den Kalkumsatz künstlich genährter Säuglinge, Jahrb. f. Kinderh., 1906, lxvi, 69.

Rousselet: Intestinal Chemism of the Alimentary Fats. Jour. Pharm. Chem., xxx, 60.

Rubner: Die Gesetze des Energieverbrauchs bei der Ernährung, Leipzig und Wien, 1902; Beiträge zur Ernährung im Knabenalter, Berlin, 1902.

Salge: Ein Beitrag zur Bakteriologie des Enterokatarrh, Jahrb. f. Kinderh., 1904, lix, 399.

Sarvonnat: Etude chimique et histologique du sclérème du nouveau-né. La Tribune méd., Sept. 21, 1907; Sur un cas de Sclérème des Nouveau-nés. Arch. de Méd. des Enf., 1906, ix, No. 1.

Schkarin: Beiträge zur Kenntnis des Säuglingsstoffwechsels bei Infektionskrankheiten, Arch. f. Kinderh., 1901, xli, Parts 1 and 2.

Schlossman: Weiteres zur Frage der natürlichen Säuglingsernährung, Arch. f. Kinderh., 1902, xxxiii, 338.

Selter: Nahrungsreste in den Säuglings fäces, Zentralbl. f. Physiol. u. Path., 1907, N. F. ii., 609.

Schelbe: Absorption of Fat by Infants, München. med. Wehnschr., 1908, 489.

Schlesinger: Disturbance of Fat Absorption and Its Relation to the Excretion of Calcium, Magnesium and Ammonia, Ztschr. f. klin. Med., 1904, lv, 214.

Schlossmann, A.: Beiträge zur Physiologie der Ernährung des Säuglings, Verhandl. d. Versamml. d. Gesellsch. f. Kinderh., deutsch. Naturf. u. Aerzte (1909), Wiesb., 1910, 67.

Shaw and Gilday: A Study of the Absorption of Fats in Infants, Brit. Med. Jour., 1906, No. 2, 932.

Siebert: Ueber das Verhalten der festen und flüssigen Fettsäuren im Fett des Neugeborenen und des Säuglings, Hofm. Beitr., i, 183.

Sommerfeld: Zur Kenntnis der Magensaftsekretion nebst einigen Bemerkungen über Speichelsekretion, Arch. f. Kinderh., 1908-9, xlix, 1.

Soxhlet: Die Erzeugung fettreicher milch, Ref. Malys Jahresb. d. Tierschemie, 1896, No. 2.

Steinitz: Zur Kenntnis der chronischen Ernährungsstörungen der Säuglinge, Jahrb. f. Kinderh., 1902, lvii, 689; Ueber den alimentären Einfluss des Fettes auf die renale ammoniakausscheidung, Zentralbl. f. inn. Med., 1904, No. 3.

Steinitz und Weigert: Ueber den Einfluss einseitiger Ernährung mit Kolehhydraten auf die chemische, Zusammensetzung des Säuglingskörpers, Hofm. Beitr., vi, 206; Ueber die chemische Zusammensetzung eines ein Jahr alten atrophischen und rachitischen Kindes, Monatschr. f. Kinderh., 1905-6, iv, 1.

Teireira de Mattos: Die Buttermilch als Säuglingsnahrung, Jahrb. f. Kinderh., 1902, lv, 1.

Terrione, E. F.: Zur Kenntniss der Fettspaltung durch Pankreassaft, Biochem. Ztschr., 1910, xxiii, 404.

Thiemich: Ueber die Herkunft des fötalen Fettes, Zentralbl. f. Physiol., xiii, 850; Jahrb. f. Kinderh., lx, 174; Zur Kenntnis der Fette im Säuglingsalter und der Fettleber bei Gastroenteritis, Ztschr. f. physiol. Chem., 1898-9, xxvi, 189.

Tobler: Ueber die Verdauung der Milch im Magen, Ergebn. d. inn. Med. u. Kinderh., 1908, i, 288.

Tschernoff: Ueber sogenannte Fettdiarrhoea nach Demme und Dr. Biedert, Jahrb. f. Kinderh., 1885, xxii, 1.

Uffelmann: Ueber den Fettgehalt der Faeces gesunder Kinder des ersten Lebensjahres und über die Ausnutzung des Fettes Seitens derselben bei Verschiedener Ernährung, Arch. f. Kinderh., 1881, ii, 1.

Uffenheimer: Die arbeiten des Finkelsteinschen Schule über Ernährungspathologie und Ernährungs therapie des Säuglings, Monatschr. f. Kinderh., 1910, ix, No. 7, 265.

Usuki: Das Schicksal des Fettes im Darm des Säuglings unter normalen und pathologischen Verhältnissen, Jahrb. f. Kinderh., July, 1910, 19.

Volhard: Ueber Resorption und Fettspaltung im Magen, München. med. Wehnschr., 1900, p. 141; Ueber die Untersuchung des Pankreassaftes beim Menschen und eine Methode der quantitativen Trypsin bestimmung, München. med. Wehnschr., 1907, p. 403.

Wegscheider: Ueber die normale Verdauung bei Säuglingen, In-Dissert., Berlin, 1875.

Weigert: Ueber den Einfluss der Ernährung auf die chemische Zusammensetzung des organismus, Jahrb. f. Kinderh., 1905, lxi, 178; Ueber den Einfluss der Ernährung auf die Tuberculose, Berl. klin. Wehnschr., 1907, No. 38.

Wells, John W.: The Digestibility of Fats and Oils, with Especial Reference to Emulsions, Brit. Med. Jour., 1902, x, 18.

Wentworth: Utilization of Milk Fat by an Atrophic Infant, Arch. Int. Med., Oct. 15, 1910.

Wilson, G. E.: Absorption of Fat in the Intestines, Tr. Canadian Inst., 1906, viii, 241.

THE BACTERIOLOGY OF THE BLOOD IN EARLY LIFE *

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Medical literature is full of reports of the bacteriologic examinations of the blood in adults, and much valuable information has been obtained therefrom. Various infections have been studied in this way: typhoid, pneumonia, endocarditis, erysipelas, osteomyelitis, and many of the obscure febrile cases so frequently seen in our hospital wards. But while much work of this nature has been done among adults, we find comparatively few reports on this subject among infants and children. In scarlet fever alone have bacteriologic examinations of the blood been made to any extent.

Study of this infection by Jochmann,¹ Baginsky, Slavyk,² Hektoen³ and others, has shown the presence of a streptococcus, apparently identical in its characteristics with the streptococcus erysipelatis. Thus, Jochmann, studying 161 cases of scarlet fever, found the streptococcus twenty-five times. All of these patients died, and Jochmann, from analysis of his own cases and those of other authors, comes to the conclusion that the presence of this organism in the blood in scarlet fever gives an almost fatal prognosis. Curiously enough, however, neither Jochmann nor Slavyk found the streptococcus in the foudroyant cases, also invariably fatal.

Aside from these studies on scarlet fever, reports on other infections in children are meager. Rotch and Low⁴ report a series of thirty-six cases comprising a variety of infections, the greatest number of any single infection being typhoid (eight). They point out the scientific and practical value of taking blood cultures and urge a more widespread use of this method of investigation.

Delestre⁵ examined the blood in forty cases, the patients ranging in age from a few days up to 4 years, all suffering from infections likely to prove fatal. Thirty-two of the forty died; eight recovered. Among the eight recoveries there was but one infant showing an organism in the blood, and this organism was the influenza bacillus. In the fatal cases, the blood obtained either during life or immediately after death, showed

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1. Jochmann: *Deutsch. Arch. f. klin. Med.* 1903, lxxviii, 209. *Ztschr. f. klin. Med.* 1904, liv, 408.

2. Slavyk: *Jahrb. f. Kinderh.*, liii, No. 5.

3. Hektoen: *Jour. A. M. A.*, 1903, xl, 685.

4. Rotch and Low: *Jour. Am. Med. Assn.*, 1907, xlviii, 185.

5. Delestre: *Ann. d. gynéc. et obst.*, 1901, lv, 51.

organisms in twenty-two, in order of frequency as follows: streptococcus, staphylococcus, pneumococcus and colon bacillus.

Delestre also examined the blood from twenty-one premature infants; of these nineteen died, and fifteen of the fatal cases showed organisms in the blood, the order of frequency being as follows: streptococcus, colon bacillus, staphylococcus and pneumococcus. The author attributes this susceptibility of the newly-born to bacteremia, to the extensive absorbing surface in the lungs and intestines, and regards these tracts as the main points of entry of the bacteria, though the umbilicus, of course, is another vulnerable point. He gives few details in his cases, not stating either the clinical or anatomic diagnosis. The blood taken during life was obtained by an incision into the skin, and he believes his technic was so nearly aseptic that there was no danger of contamination.

Otten⁶ reports a series of 250 cases of lobar pneumonia in children up to 15 years of age, with blood-cultures in seventy. He found the pneumococcus in nine of these seventy cases, 13 per cent.; of these nine, four patients recovered; five died.

The paucity of studies on this important subject in children is undoubtedly due to the difficulty of obtaining sufficient blood for examination from this class of patients. The veins of children are so small that it is extremely difficult to get into them. We have ourselves experienced this difficulty, and, besides the cases reported below, have made numerous but unsuccessful attempts to obtain the blood from other patients, chiefly infants and young children. Others apparently have had the same experience. Indeed, one author, studying a large series of infections of otitic origin among adults, "throws up the sponge" at the outset and says that no attempt is made to study children on account of the difficulty of carrying out the technic. But considering the frequency of obscure febrile infections among infants and children, it would seem that in such patients especially, systematic bacteriologic blood-examinations might be of great value; furthermore, in view of the future possibilities of antivaccine and antiserum treatment, accurate knowledge of disease is more than ever desirable; hence any method of investigation which promises to give us this accurate knowledge should be thoroughly tested, and, if prolific of results, systematically employed. It seems worth while, therefore, to report the following cases, even though small in number:

TECHNIC

Most of the cases have been studied at the Children's Memorial Hospital, a few each at the Cook County and Presbyterian hospitals, and to the attending physicians at these institutions we are much indebted for the material used.

6. Otten: *Jahrb. f. Kinderh.*, 1909, *lxi*, 568.

The blood has been obtained by the usual method, from the median basilic vein just above the elbow. In two cases of suspected typhoid it was obtained from the lobe of the ear, as recommended by Peabody. Various kinds of syringes have been used, but the Luer glass-syringe has been the most satisfactory. The blood thus obtained has been mixed immediately at the bedside with various media: in most of the cases two tubes of bouillon, two of agar and agar plate have been inoculated. In five of the typhoid cases, ox-bile has been used as the medium, with positive results in all. A case of suspected typhoid in which bile medium was used was negative, but proved later to be a case of tuberculous meningitis.

In using the ox-bile as a medium, the following technic was observed:

Test tubes containing fresh ox-gall sterilized in the autoclave were used. The blood obtained from the vein, or from the lobe of the ear in some cases, was introduced directly into the test-tube of bile. This was then put in the incubator from fifteen to eighteen hours, at the end of which time a few loopfuls were transferred to a tube of coagulated blood-serum: after three to five hours of incubation microscopic examination of the water of condensation showed, in the positive cases, the presence of motile bacilli. The presence of such motile bacilli is now accepted as evidence of a typhoid or a paratyphoid organism.

We have made sixty-nine examinations on sixty-four infants and children during life, and have studied sixteen cases post mortem. It is with the former group of cases that we are chiefly concerned. This is composed of the following infections:

Disease	No of Cases	Results
Typhoid	20	11 Positive
Pneumonia—		
Lobar	15	3 Positive
Lobular	3	1 Positive
Rheumatism	5	5 Negative
Meningitis—		
Meningococcus	5	2 Positive
Staphylococcus	1	1 Negative
Tuberculous	1	1 Negative
Chorea	2	2 Negative
Pyelitis	2	2 Negative
Nephritis	1	1 Negative
Erysipelas	1	1 Negative
Appendicitis, General peritonitis and lobar pneumonia	1	1 Negative
Leukemia	1	1 Positive
General septicemia	1	1 Positive

In addition to the above one case each of scorbutus, miliary tuberculosis, arthritis deformans, toxic erythema and of tuberculous adenitis, gave negative results. Thus, of the sixty-nine examinations made on these sixty-four children, we have obtained nineteen positive results. These will now be analyzed according to individual infections.

TYPHOID

It is in this infection perhaps that the greatest amount of blood-culture work has been done among adults, with interesting and important results. During the first week of the disease, 95 to 100 per cent. of the patients will show the presence of typhoid bacilli in the circulating blood: with the progress of the disease, this number diminishes so that in the second or third week they are found much less frequently (40 per cent.). As the Widal reaction pursues exactly the reverse course, absent at first, present later, the blood culture test becomes an extremely important method in the early diagnosis of typhoid, at least among adults.

How is it among children? Our own cases are of course too few to warrant conclusions. We can state only that eleven of the twenty cases gave positive results, and that these positive results were obtained as early as the sixth and as late as the twenty-second day (Table 1). The negative results were obtained in the first case on the tenth, thirteenth and twentieth days, in the second case during the seventh week (relapse), and in the third and fourth cases on the eighth day.

Combining Rotch's series, our own and a few scattering reports in literature, we find thirty-one cases of typhoid fever, in twenty, or 66 per cent. of which, bacilli were found in the circulating blood. We find, furthermore, that they were found as early as four days before the onset of symptoms and as late as the twenty-second day. The former case was that of a 12-year-old child whose sister was already ill with typhoid (Conradi).⁷

These results were obtained with all kinds of media and at all periods of the disease. It is probable that with the more widespread use of Conradi's ox-bile medium and more frequent examinations early in the disease, this proportion of positive results will be considerably increased. Only when large numbers of cases have been examined, and at different periods of the disease, can we draw final conclusions as to the importance of this particular laboratory investigation. If the results of the future correspond with the results already obtained in large numbers of adults, this method will become even more valuable among children on account of the more irregular, atypical nature of the disease in early life. We urge a constant, widespread use of the method, that our knowledge in this direction may be increased as rapidly as possible.

PNEUMONIA

The pneumococcus is a frequent invader of the blood in adults, not only in pneumonia, but also in pneumococcic infections with the pathologic seat of the disease in other localities, e. g., the endocardium and pericardium, the joints, the meninges, the tonsils, etc. As in typhoid the literature is voluminous as to adults, meager as to children.

7. Conradi: *Deutsch. med. Wchnschr.*, 1906, xxxii, 58.

Otten studied 250 cases of pneumonia in children up to 15 years of age. He made blood-cultures on seventy of these patients, finding the pneumococcus in nine, or 13 per cent. Of these nine children four recovered, five died.

Spitta⁸ describes a case of lobar pneumonia in a 17 months' infant, with a general pneumococcic infection, resulting in an arthritis and empyema; pneumococci were found in the blood during the sixth week of illness and one week before death. Autopsy confirmed the antemortem examinations.

We have taken cultures in fifteen cases of lobar pneumonia and three of lobular pneumonia. Four of the cases in the former group were positive, one in the latter, the organism found being the pneumococcus in every instance.

Thus in the eighty-five cases comprising our own and Otten's series, thirteen, or 15 per cent., showed pneumococci in the circulating blood, a striking difference from its frequency among similar infections in adults. This failure to discover the organism more frequently in the blood in children is due to one of the two causes. Either the technic employed in the cases already studied is faulty, or the organism does not invade the blood frequently. The technic employed is apparently important, great discrepancies existing among the authors who have studied this question in adults. Thus Lenhartz, Schottmüller, Grimm and Jochmann find pneumococci in the blood in only one-fourth to two-thirds of their cases, whereas Procharska and Weins find them in practically *all* of their cases. The former group of observers worked with solid media—blood-agar; the latter with fluid media—blood bouillon.

To this difference in culture media, Otten attributes the varying results obtained by these workers, maintaining that the pneumococcus grows better on fluid media, and that consequently those who use such media will get a comparatively high percentage of positive results. He himself in his work on children used fluid media, yet got positive results in only 13 per cent. of his cases. Consequently, if his reasoning be correct, the pneumococcus is not a frequent invader of the blood in the lobar pneumonia of children. However, here again the cases available for study are too few to warrant final conclusions, either as to the frequency of its appearance or as to its prognostic value when present. Future investigations must determine these points.

THE RHEUMATIC AFFECTIONS

In this group we have included cases of endocarditis, arthritis, tonsillitis and chorea, these manifestations occurring either singly or in combination with each other (Table 1).

8. Spitta: Brit. Med. Jour., 1902, ii, 1579.

TABLE 1.—BACTERIOLOGY OF BLOOD ANTE-MORTEM

Case, Sex and Age	Clinical Diagnosis	Day of Disease	Number of Cultures	Medium	Result	Remarks
1—M.—4 years.	Typhoid	?	1	Agar plate; two bouillon.	Negative.	Three Widal's incomplete; persistent leukopenia; recovery.
2—M.—7 years.	Typhoid	10-13-20th day.	3	Bile	All negative.	Recovery; Widal positive tenth day.
3—M.—12 years.	Typhoid	14th day.	1	Bile	Positive.	Recovery; Widal positive.
4—F.—11 years.	Typhoid	6th day.	1	Bile	Positive.	Recovery; Widal negative fourth day; culture taken second day of menses.
5—M.—42 months.	Typhoid	7th day?	1	Bile	Positive.	Entered hospital for genu valgum; blood from ear third day of a measles rash; Widal negative sixth day.
6—F.—5 years.	Typhoid	22d day.	1	Bile	Positive.	Recovery; Widal negative twenty-first day.
7—F.—10 years.	Typhoid	?	1	Bile	Positive.	Recovery; severe case; hemorrhages.
8—F.—11 years.	Typhoid	10th day.	1	..	Positive.	Negative during relapse; recovery; Widal positive eighth day.
9—M.—6 years.	Typhoid	7th week.	1	..	Negative.	Recovery; Widal positive fifteenth day.
10—F.—8 years.	Typhoid	14-18th day.	2	..	Both positive.	Recovery; Widal positive fifth day.
11—M.—5 years.	Typhoid	6th day.	1	..	Positive.	Recovery; Widal positive eighth day; serum reaction to "paracolony" B. and "paratyphoid" B. negative.
12—M.—12 years.	Typhoid	8th day.	1	..	Negative.	Widal negative fifteenth and seventeenth days.
13—M.—11 years.	Typhoid	3d week.	1	..	Positive.	Widal positive eighth day.
14—M.—4 years.	Typhoid	15th day.	1	..	Negative.	Widal positive.
15—M.—42 months.	Typhoid	8th day.	1	..	Negative.	Widal positive.
16—M.—6 years.	Typhoid	7-12th day.	2	..	Negative.	Widal positive; recovery.
17—F.—8 years.	Typhoid	9th day.	1	..	Positive.	Widal positive; recovery.
18—F.—8 years.	Typhoid	6th day.	1	..	Positive.	Widal positive; recovery.
19—M.—10 years.	Typhoid	10th day.	1	..	Negative.	Widal positive; recovery.
20—F.—10 years.	Typhoid	15th day.	1	..	Negative.	Widal positive; death.
21—M.—18 months.	Pneumonia	?	1	..	Negative.	Second day of a high temperature probably a relapse; outcome unknown; child removed from hospital against advice.
22—M.—30 months.	Pneumonia	?	1	..	Negative.	Recovery.
23—M.—7 years.	Pneumonia	15th day.	1	..	Negative.	Lysis on fifteenth to sixteenth day; recovery.
24—M.—9 years.	Pneumonia	10th day?	1	..	Negative.	Appendicitis; general peritonitis; pneumonia; death.
25—F.—2 years.	Pneumonia	8th day.	1	..	Positive.	Rhinitis; temperature normal ninth day; convalescence tedious; recovery in two months.
26—M.—3 years.	Pneumonia	8th day.	1	..	Negative.	Crisis on ninth day; recovery.
27—M.—2 years.	Pneumonia	4th day.	1	..	Negative.	Brother and sister on same day; pneumococci in sputum of each.
28—M.—5 years.	Lobar pneumonia	5th day.	1	..	Positive.	Recovery.
29—F.—7 years.	Lobar pneumonia	4th day.	1	..	Positive.	Recovery.
30—M.—9 years.	Lobar pneumonia	9th day.	1	..	Negative.	Recovery.
31—M.—18 months.	Lobar pneumonia	4th day.	1	..	Positive.	Recovery.
32—F.—6 years.	Lobar pneumonia	7th day.	1	..	Negative.	Recovery.
33—F.—9 years.	Lobar pneumonia	4th day.	1	..	Negative.	Recovery.
34—M.—11 years.	Lobar pneumonia	4th day.	1	..	Negative.	Recovery.
35—F.—12 years.	Lobar pneumonia	9th day.	1	..	Negative.	Chronic endocarditis; recovery from pneumonia.
36—M.—1 year.	Lobular pneumonia.	10th day.	1	..	Negative.	Recovery.

37—F.—16 months.	Lobular pneumonia.	2d week. ?	1		Negative..	Pneumococci in blood.
38—M.—20 months.	Lobular pneumonia.	Weeks.	1		Positive..	Death.
39—F.—54 months.	Pulmonary abscess.	? 17 ?	1		Negative..	Streptococci in blood and in pus from abscess; removed from hospital.
40—F.—11 years.	Chronic endocarditis.	? 3d-11th day.	1	Blood agar; bouillon.	Negative..	Acute exacerbation; culture taken two months before death.
41—M.—4 years.	Chronic endocarditis.	? 3d-11th day.	2		Negative..	During intercurrent tonsillitis (streptococcus).
42—F.—6 years.	Chronic endocarditis.	? 3d-11th day.	1		Negative..	Culture second day of a three days' temperature; no evident cause; recovery from this.
43—M.—11 years.	Chronic endocarditis.	Months.	1	Agar bouillon....	Negative..	Antecedent history of rheumatism; entered C. M. H. 3-19-10; temperature, 98-103 from 3-27-10 to 4-7-10; culture taken 4-1-10; temperature 99-102 that day.
44—F.—11 years.	Chorea; chronic endocarditis.	7th week.	1	Agar bouillon....	Negative..	No elevation of temperature; recovery.
45—M.—10 years.	Chorea; chronic endocarditis.	19th day.	1		Negative..	Antecedent rheumatism; culture taken after three-four days' temperature without evident cause, when it became normal.
46—F.—66 months.	Rheumatic fever.	9-16th day.	2		Negative..	Chronic (?) endocarditis and arthritis; improvement, then measles, acute tonsillitis (streptococcus and staphylococcus), general septicemia; death; cultures during acute arthritis, etc.
47—M.—3 years.	Meningitis	5th day.	1		Negative..	Meningococcus in spinal fluid; death one month later.
48—M.—10 years.	Meningitis	? 7th day.	1		Positive..	Meningococcus in spinal fluid; death eleventh day.
49—M.—66 months.	Meningitis	5th day.	1		Negative..	Meningococcus in spinal fluid; death fifty-first day.
50—M.—9 years.	Meningitis	5th day.	1		Positive..	Meningococcus in spinal fluid; recovery.
51—F.—6 years.	Meningitis	48th day.	1	Bouillon; agar plate.	Negative..	Meningococcus in spinal fluid; death four weeks later.
52—F.—22 months.	Meningitis	12th day.	1		Negative..	Staphylococcus in spinal fluid; recovery.
53—F.—10 years.	Meningitis	10th day.	1	Bile	Negative..	Suspected typhoid; Widal negative; von Pirquet positive tenth day; spl. fl. that of tuberculous meningitis; death.
54—F.—20 months.	Pyelitis	Weeks.			Negative..	Rachitis, chronic endocarditis, otitis media two days before culture; pneumonia six weeks later; death.
55—F.—18 months.	Pyelitis	8th day.	1		Negative..	Recovery.
56—F.—8 years.	Erysipelas	5th day.			Negative..	Recovery.
57—F.—12 years.	Acute nephritis..	4th day.	1	Agar bouillon...	Negative..	Entered C. M. H. with typhoid symptoms; Widal negative fourth day; leukocytes 18,000; culture April 8, 1910; endocardial murmur April 11 and pericardial friction-rub April 12.
58—F.—10 years.	Scarbitus	25th day.	1		Negative..	Acute arthritis fifth day of fever; chorea.
59—M.—30 months.	Miliary Tb?	8th day.	1		Negative..	Recovery.
60—F.—5 years.	Arthritis deformans.	? 5th day.	1		Negative..	Positive Wassermann, but no characteristic signs of syphilis; left hospital unimproved.
61—F.—3 years.	Toxic erythema..	? 5th day.	1		Negative..	Positive Wassermann; improving.
62—F.—15 months.	Tuberculous adenitis (cervical)	? 5th day.	1		Negative..	Recovery; rachitis.
63—M.—4 years.	Leukemia (lymphocytic)	Weeks.	1		Positive..	Streptococci in blood one week before death.

Post-mortem examinations in cases of endocarditis have shown a varied bacteriology, streptococci, staphylococci, pneumococci, gonococci, pyocyaneus and influenza bacillus, all having been found in the heart's blood and on the valves of the heart in such patients. During life, in cases of septic endocarditis in adults, bacteria have often been found in the blood (Billings). We know practically nothing of this aspect of the subject in children, however. Our own group comprises seven cases; all had chronic endocarditis; in five of the cases, the cultures were taken during a febrile stage, due either to a tonsillitis, an arthritis, or to an unknown cause, possibly an acute exacerbation of the chronic endocarditis. There were two cases of chorea, and in both of these the temperature was normal when the cultures were taken. Cultures were negative in all seven of the cases.

MENINGITIS

It was formerly thought that in epidemic meningitis the meningococcus rarely invaded the blood, but recent investigations with improved technic show its presence in the blood in about 25 per cent. of the cases. We have examined four cases, with two positive results. In the tuberculous case the patient was examined on the tenth day of the disease as a suspected typhoid.

OTHER DISEASES

One case each of pyelitis, erysipelas and acute nephritis gave negative blood-cultures. Catheterized specimens of urine from the cases of pyelitis and nephritis showed a streptococcus in the former and nothing in the latter. One case of acute lymphocytic leukemia showed the streptococcus in the blood one week before death.

POST MORTEM

Much more work has been done on the bacteriology of the blood on children post mortem than ante mortem. After death the blood often shows the presence of organisms in great variety. We have reports on the bacteriology of the heart's blood in seventeen cases, of which thirteen showed positive results. These cases comprised the usual run of hospital patients: intestinal, pulmonary, bronchial, otitic, etc. (Table 2). Three cases of special interest were, one each of hemorrhagic disease of the newly born, erysipelas and status lymphaticus. The hemorrhagic disease showed in the heart's blood the *Staphylococcus aureus*, the bacillus coli, the streptococcus and an unidentified diplococcus midway between the pneumococcus and the streptococcus.

Of the four cases with a sterile heart's blood, three were as follows: A pyelo-nephritis due to the *B. pyocyaneus*, an otitis with a general septicemia, but with entirely negative post-mortem results, and a meningo-

TABLE 2.—BACTERIOLOGY OF BLOOD POST-MORTEM

Case, Sex and Age	Clinical Diagnosis	Anatomical Diagnosis	Blood—		Hours After Death	Remarks
			Ante- Mortem	Post-Mortem		
1—...—12 days.	Hem. disease of new-born.	Septic thrombosis of umbilical vessels; few numerous hemor- rhages; meningitis ileocolitis; broncho- pneumonia.	No exam- ination.	Staphylococcus aureus coli; few streptococcus.	5	All organisms in cerebrospinal and peritoneal fluids; staphylococcus and <i>B. coli</i> only in pericardial fluid.
2—F.—8 months.	Ileocolitis	Ileocolitis; broncho- pneumonia.	No exam- ination.	Streptococcus	3	Streptococcus in pericardial pleura, peritoneal and splenic fluid; staphy- lococcus aureus in bile, splenic and pericardial fluids.
3—M.—Infant.	Rachitis	Enterocolitis; rach- itic osteochondri- tits.	No exam- ination.	Smears: Gram-positive cocci and a gram-negative bacillus. Cul- tures: Staphylococcus aureus and colon bacillus.	8	
4—M.—4 months.	Malnutrition	Ileocolitis; broncho- pneumonia.	No exam- ination.	Three organisms resembling in all respects streptococcus pyogenes. Staphylococcus aureus and dip- lococcus lanceolatus.	6	Some organisms from pus of lung.
5—F.—4 months.	Gastro-enteritis ..	Gastro-enteritis; oti- tis media; bron- chitis; meningitis.	No exam- ination.	Negative	36	Cultures from cerebrospinal fluid showed the colon bacillus.
6—M.—3 months.	Broncho- pneumonia	Bronchopneumonia; cere- brospinal meningi- tis; patent ductus arteriosus.	No exam- ination.	Staphylococcus aureus; strepto- coccus pyogenes.	28	Cultures from cerebrospinal fluid showed: diplococcus lanceolatus, staphylococcus aureus, streptococ- cus pyogenes, <i>B. localis</i> alk.
7—M.—6 months.	Enterocolitis*	Enterocolitis	No exam- ination.	Staphylococcus albus	30	
8—F.—11 years.	Endocarditis		Negative.	Negative	16	Bouillon only used post-mortem.
9—F.—3 years.	Otitis; general septicemia.	Nothing abnormal found.	No exam- ination.	Negative	16	
10—M.—14 months.	Pyelonephritis....	Pyelonephritis; bronchopneumonia; cloudy swelling of myocardium, liver and kidney.	No exam- ination.	Negative	18	<i>B. pyocyaneus</i> in pelvis of left kidney; also <i>B. coli</i> ; staphylococcus albus from mesenteric gland; staphylococ- cus aureus from right ureter; staphy- lococcus citreus and micrococcus tetragenus from pericardium.
11—F.—5 months.	Enterocolitis	Enterocolitis	No exam- ination.	Staphylococcus albus	50	
12—F.—18 months.	Meningitis	Status lymphaticus.	No exam- ination.	A diplococcus midway between the micrococcus and the strepto- coccus pyogenes; colon bacillus; streptococcus.	1	No meningitis.
13—F.—20 months.	Rachitis; pye- litis; endocardi- tis; laryngitis; lobar pneumonia	Rachitis; acute nephritis; vegeta- tive endocarditis; laryngitis; lobar pneumonia.	Negative.	Contamination?	..	Colon bacillus on trachea. (Case 56, Table 1.)
14—M.—3 months.	Enterocolitis		No exam- ination.	Streptococcus	..	
15—...—3 months.	Erysipelas	Pulmonary tubercu- losis.	No exam- ination.	Streptococcus	15	
16—F.—6 months.	Lobar pneumonia	Purulent meningitis.	No exam- ination.	Negative	..	Meningococci in spinal fluid, ante- mortem.
17—M.—.....	Meningitis (men- ingococcus). Infant atrophy ..	Lobular pneumonia; patent foramen ovale.	No exam- ination.	Negative	24	

coccic meningitis. The fourth case was an endocarditis in which the ante-mortem blood was also sterile (Case 26, Table 2).

The organisms recovered post mortem were as follows: the staphylococcus six times, aureus five times, albus one time, the streptococcus eight times, bacillus coli three times, the *Diplococcus lanceolatus* one time, and the unidentified diplococcus already mentioned.

We are much indebted to Prof. E. R. LeCount of the Pathological Department of Rush Medical College, under whose supervision most of the post-mortem work in our cases was done.

SUMMARY

The main points in this paper may be briefly summarized as follows:

Blood-cultures in adults during life, in large numbers of cases, have yielded information of scientific interest and diagnostic value.

Little work in this direction has been done in the infections of early life. There is need of more of this work among infants and children.

It is reasonable to suppose that blood-cultures in early life may be of even more value than in adult life, on account of the greater frequency of obscure infections during the former period.

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THE METABOLISM OF NITROGEN, PHOSPHORUS AND
THE PURIN SUBSTANCES IN THE NEW-BORN; WITH
SPECIAL REFERENCE TO THE CAUSATION OF
THE URIC ACID INFARCTS OF THE KIDNEY *

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I. INTRODUCTION

During the first few days in the life of an infant a number of phenomena may occur which border closely on the pathologic, among which is the frequent, if not constant, deposit of uric acid or its salts in the kidney tubules. Numerous investigations have been directed toward the solution of the etiology of this condition, in spite of which a number of the factors concerned are still obscure. Our own investigation was undertaken in the effort to determine the uric acid output, the factors on which it depends, and certain related problems of metabolism in the new-born infant.

It is a common observation that the urine of the new-born is often turbid and frequently leaves a deposit of uric acid or urates on the napkin; and in a large percentage of the infants who die during the first few days of life, a deposit of uric acid or urates¹ is found in the medullary portion of the kidney—the so-called uric acid infarcts. It has been observed that these deposits are rarely present in dead-born infants; that they are found with greatest frequency in infants dying between the second and eighth days of life, and that their occurrence is infrequent after the twentieth day.

In 282 autopsies on living-born infants collected by Hodann,² infarcts were present in 117 cases (42 per cent.). Hecker³ noted their presence in 40 per cent. of infants who had lived from a few hours to two months. Salomenson's⁴ statistics show their presence in 39 per cent. of 462 living-born infants.

* From the Laboratory of Biological Chemistry of Columbia University at the College of Physicians and Surgeons, New York, and the New York Nursery and Child's Hospital.

1. Reusing and Ebstein considered that the uric acid was deposited as such. Parrot and Salomenson believed that it occurred as sodium urate, while Flensburg and Virchow thought that the infarct salt was ammonium urate. The analysis of Sjöqvist indicates that the uric acid is deposited as acid ammonium urate, or perhaps a mixture of this salt and neutral ammonium urate.

2. Quoted by Czerny and Keller: *Des Kindes Ernährung, Ernährungsstörungen*, etc., 1906, p. 167, etc.

3. Hecker: *Virchow's Arch. f. path. Anat.*, 1857, xi, 217.

4. Salomenson: Quoted by Flensburg.

It was shown by Martin and Ruge,⁵ Parrot and Robin,⁶ Virchow,⁷ Hofmeier,⁸ Ebstein,⁹ Flensberg¹⁰ and others that the infarct elements—hyaline or granular cylinders or spheres incrustated with uric acid or urates—are frequently present in the urine of the new-born and are identical with those found in the kidney. In sixty-three observations on infants from birth to 8 days of age by Hofmeier, these elements were found in 62 per cent.¹¹ In the reports collected by Flensberg, their presence was noted for the urines of 101 (58 per cent.) of 173 infants from birth to the sixth day of life. They were present in nearly 90 per cent. of the cases in which the urine was examined during the last half of the first day and during the second day of life. The results were positive in all of the twenty infants examined by Flensberg. These results led Flensberg to believe that the causation of such infarcts is a physiologic process and occurs to some degree in all new-born infants.

A great number of hypotheses have been advanced to explain the causation of the infarcts. Schlossberger¹² considered that intestinal disturbances gave rise to an increased excretion of uric acid, and that a sedimentation of the urine was induced by a contraction of the urinary tubules, due to a low body temperature. Virchow⁷ attributed their occurrence to the revolution of metabolism which occurred at birth. Miller¹³ sought their explanation in a low temperature, insufficient respiration and oxidation, and renal congestion due to increased work thrown on the heart. Vierordt¹⁴ considered that the feeble powers of oxidation, and the concentration of the urine due to the small fluid intake, were the important factors. Coming to the more specific explanations we have that of Ebstein⁹ who thought that there was a primary deposit of uric acid which caused a necrosis of the kidney parenchyma, and thus gave rise to the infarct stroma. The uric acid excretion in the new-born was determined by Reusing¹⁵ who found that it was very high. He considered that this high uric acid output, and the high acidity of the urine were the predisposing factors; the exciting cause was the great concentration of the urine due to the deficient fluid intake. Sjöqvist¹⁶ deter-

5. Martin and Ruge: *Ztschr. f. Geburtsh. u. Frauenkr.*, 1876, i, 273.

6. Parrot and Robin: *Arch. gén. de méd.*, 1876, i, 129, 309.

7. Virchow: *Gesammelte Abhandlungen zur wissenschaftl. Med.*, 1856, p. 833.

8. Hofmeier: *Virchows Arch. f. path. Anat.*, 1882, lxxxix, 493.

9. Ebstein: *Die Natur und Behandlung der Harnsteine*, Wiesbaden, 1884.

10. Flensberg: *Nörd. Med. Ark.*, 1894, No. 9, N. S.; *Centralbl. f. inn. Med.*, 1894, xv, 965.

11. Hofmeier found the infarcts in a much larger percentage of infants whose mothers had been chloroformed during labor.

12. Schlossberger: Quoted by Czerny and Keller, p. 160.

13. Miller: *Jahrb. f. Kinderh.*, 1886, xxv, 187.

14. Vierordt: *Gerhardt's Handbuch der Kinderkrankheiten*, 1877, i, 147.

15. Reusing: *Ztschr. f. Geburtsh. u. Gynäk.*, 1895, xxxiii, 36.

16. Sjöqvist: *Nörd. Med. Ark.*, 1894, No. 10, N. S.; *Maly's Jahresb.*, 1894, xxiii, 245.

mined the uric acid in catheterized specimens of urine obtained by Flensburg, and found that there was a great increase during the infarct period—the last half of the first day and the second day of life. Flensburg¹⁰ considered that the exciting cause of the infarcts was the excretion of an albuminous material into the tubuli contorti during fetal life and shortly after birth. The casts which formed the groundwork for the infarcts were thus developed, and, coming in contact with the concentrated urine, received a deposit of uric acid.

The problem of the etiology of this condition presents, therefore, two important phases for solution. First, the cause for the high uric acid output shown by Reusing and Sjöqvist, and next, the cause for the deposit of uric acid in the kidney tubules. It was toward the solution of the former that this investigation was especially directed.

II. EXPERIMENTAL

Technic.—Observations were conducted on nine full term, male infants who were nursed by their own mothers. Labor was normal in all cases. The mothers received only small amounts of chloroform; never enough to induce narcosis, and rarely more than 30 c.c. All of the infants were apparently normal at birth and remained so during the period of observation. Two of the infants showed a very mild degree of jaundice (Protocols IV and VI).

The urine was collected by means of a drawn out test-tube which was fastened over the well lubricated penis, and connected by means of glass and rubber tubing to a bottle attached to the side of the crib. Powdered thymol was used as a preservative. The glass tube was attached by means of wool knitting floss and adhesive plaster. The floss strands were arranged so as to encircle the body and thighs; the adhesive plaster was used to attach the glass tube to the floss bands. The method has the advantage that the adhesive plaster does not touch the delicate skin of the infant, thus avoiding all irritation; that it can be used in circumstances where restraint is not permitted; and that the apparatus needs no readjustment at the time of maternal nursing. It has the great disadvantage that part of the urine may be lost unless the infant is closely watched, and unless the body is elevated or the glass tube fastened to the napkin and set slantingly so that there is a gradual incline from the penis to the collecting bottle. To obviate this difficulty the infants were kept on their sides and the tube included in the portion of the napkin which passed around the lower thigh. As a further precaution, a layer of absorbent cotton was wrapped around the upper end of the glass tube so that any leakage of urine could be easily detected. Occasionally, edema of the prepuce developed, but in most instances it was slight and was due to insufficient lubrication of the penis, or the tube was fastened so tightly around the base of the penis that it interfered with the circulation. The edema usually subsided promptly on correction of the underlying fault.

but in two instances it was sufficiently severe to require removal of the apparatus before the conclusion of the experiment. The feces were collected by means of thin rubber napkins and were washed into a suitable receptacle with small quantities of distilled water.

The uric acid was determined by the method of Folin and Shaffer,¹⁷ the acidity by the method of Folin,¹⁸ the total nitrogen by the Kjeldahl process, and the purin content of the milk and feces by the method of Krüger and Schittenhelm.¹⁹ Phosphorus was determined gravimetrically as magnesium pyrophosphate after oxidation by the method of Neumann.²⁰ The method for the purin bases varied depending on the amount of urine available. Either Kenneway's modification of the Cammerer-Arnstein method,²¹ or the method of Krüger and Schmid²² was used. In the latter the precipitation was made from an acid solution as advised by Benedict and Saki.²³ The specific gravity was determined with a small hydrometer standardized against distilled water.

The determinations were made in duplicate whenever the amount of material permitted, and all procedures were carefully checked. Blank nitrogen determinations were made with each series and the results deducted from the actual determinations. The leukocytes were counted by means of the Thoma-Zeiss apparatus and the counts were made at the same time each day—directly before a nursing.

As a matter of convenience the periods were taken from 9 a. m. to 9 a. m. The first day period varied, but extended from the time of birth to 9 a. m. the next day, when this period approximated twenty-four hours, and when the amount of urine was sufficient for examination. Otherwise the period was extended another twenty-four hours. The exact time in each case is shown in the protocols.

The urine of the first few days often contained a sediment which it was necessary to dissolve before proceeding with the chemical examination. This was done by diluting with hot distilled water and adding, when necessary, a few drops of a 1 per cent. solution of sodium hydroxid.

It has been shown by Budin,²⁴ Rebemont,²⁵ Shücking,²⁶ Schiff,²⁷ Hofmeier²⁸ and others that the total blood mass of the new-born infant may be influenced to a considerable degree by the time of ligation of the umbil-

17. Folin: *Am. Jour. Physiol.*, 1905, xiii, 49.

18. Folin: *Am. Jour. Physiol.*, 1905, xiii, 53.

19. Krüger and Schittenhelm: *Abderhalden's Handbuch der Biochemie*, 1910, iii, 893.

20. Sherman: *Organic Chemical Analysis*, 1905.

21. Kenneway: *Jour. Physiol.*, 1909, xxxix, 296.

22. Krüger and Schmid: *Ztschr. f. physiol. Chem.*, 1905, xlv, 1.

23. Benedict and Saki: *Jour. Biol. Chem.*, 1909, vii, 27.

24. Budin: Quoted by Rebemont (see note 25).

25. Rebemont: *Arch. de Tocologie*, 1879, vi, 572.

26. Shücking: *Berl. klin. Wehnschr.*, 1877, xiv, 5.

27. Schiff: *Jahrb. f. Kinderh.*, 1892, xxxiv, 159; *Ibid.* 1893, xxxv, 21.

28. Hofmeier: *Ztschr. f. Geburtsh. u. Gynäk.*, 1897, iv, 114.

ical cord. By various means, it has been determined that when the infant is left attached to the placenta some time after birth, it receives from 38 to 100 grams more blood than when the cord is ligated immediately after birth. According to Hofmeier the infant's blood mass may be thus increased by about one-third. Since it is only rational to suppose that there would be differences in the physiology of the new-born infant, dependent on the time of ligation of the umbilical cord, some of which have been shown by Hofmeier,²⁸ Schiff²⁷ and Reusing,¹⁵ our cases have been divided into two series. In one series of four cases the umbilical cord was ligated immediately after birth, in the other five cases the infants were left in contact with the placenta for from two to five minutes after the pulsation of the cord had ceased.

Quantity and Physical Characteristics of the Urine.—The quantity of urine excreted, its relation to the fluid intake, and the specific gravity of the urine have been determined by a number of observers (Parrot and Robin,⁶ Martin and Ruge,⁷ Schiff,²⁷ Reusing,¹⁵ Hofmeier,²⁸ Cruse²⁹ and others), and from much larger series of cases than we have had at our disposal. For this reason it is unnecessary to give detailed consideration to these characteristics. In conformity with the results of Hofmeier, Schiff and Reusing, the late ligation cases showed a greater urine excretion during the first few days than did the early ligation cases.

In all of our cases the appearance of the urine was noted, and the sediment, when present, or, in its absence, a centrifugalized specimen was examined microscopically. Epithelial cells and granular and hyaline casts were present in all cases at some time during the first four days. In all cases the urate spheres or uric acid cylinders were found at one time or another during the first three days. If the presence of the infarct elements in the urine signifies the occurrence of infarction—which there is no reason to doubt—our results agree with those of Flensburg, and indicate that the deposit of uric acid in the kidney is a regular occurrence in the new-born infant.

Uric Acid.—Reusing¹⁵ determined the total uric acid elimination in the new-born by the method of Hopkins, and Sjöqvist,¹⁶ the percentages by the Ludwig-Salkowski method. The uric acid values obtained by Reusing, Sjöqvist and those from our cases are shown in Table 1.

The values of Reusing are practically constant, with the exception of the increased excretion on the third day. Reusing explained this increase on the basis of the increased amount of urine excreted on this day, which was thus able to dissolve larger amounts of uric acid. Our values are higher than those of Reusing during the first four days; for the fifth, sixth and seventh days the average excretion was greater in Reusing's cases. A further and more important difference arises from the fact that while the average excretion in Reusing's cases was almost constant, with

29. Cruse: *Jahrb. f. Kinderh.*, 1877, xi, 393.

the exception of the third day, ours showed a rapid increase during the second and third days and then a diminution.³⁰ The relatively high excretion of uric acid in infancy is readily seen when the values in Table 1 are compared with the adult values of 300 to 600 mg. of endogenous uric acid per day (Burian and Schur).

TABLE 1.—THE URIC ACID ELIMINATION IN THE NEW-BORN

Day.	Average Daily Excretion of Uric Acid in Mg.		Sjövqvist.	
	Reusing, 6 Cases.	Schloss-Crawford, 8 Cases.		Uric Acid per 100 c.c. Mg.
1	41.1	59.3	1. Mixed urine of 20 infants, first 12 hours of life.	82
2	41.1	75.5	2. Mixed urine of 20 infants during second half of first day and during the second day.	232
3	83.1	91.0	3. Mixed urine of 20 infants, 5 to 7 days old.	20.3
4	39.5	62.3	4. Mixed urine of 4 infants, 5, 6 and 7 days old.	10.4
5	56.6	42.7		
6	46.3	36.4		
7	37.3	36.1		
8	...	36.0		
9	...	29.3		

The percentage determinations of Sjövqvist cannot be accurately compared with those of Reusing or ourselves, owing to the difference in the periods. His results, however, show a close relationship between the uric acid elimination and the occurrence of the infarcts. The uric acid was comparatively low before the infarct period, rose to a high level during the infarct period, and then sank to its lowest value. This relationship is also shown by our results when they are arbitrarily divided into three-day periods (Table 2).

TABLE 2.—THE URIC-ACID ELIMINATION DURING THREE-DAY PERIODS

Period.	Average Excretion of Uric Acid, Mg.
1. First, second and third days.....	75.2
2. Fourth, fifth and sixth days.....	47.1
3. Seventh, eighth and ninth days.....	33.8

Nieman³¹ has determined the uric acid output in a new-born infant and the results are approximately the same as those in our cases. Nieman found, however, only a trace of uric acid during the first day, while the maximum excretion of 99.07 mg. occurred on the fourth day. After the fourth day the uric acid excretions in this case, and in two others—one

30. In the individual cases the uric-acid excretion varied rather widely, but was usually lower on the first than on the second or third day. This, however, is not without exception (Protocols VII and VIII). These variations are due, in part, at least, to the fact that our first-day period often consisted of more than twenty-four hours. From the end of the first day the numbered days were exactly twenty-four hours each, but owing to the variations in the first day, the later days as numbered in the protocols and tables do not always indicate the exact time from birth.

31. Nieman: *Jahrb. f. Kinderh.*, 1910, lxxi, 286.

an infant of 6 days, the other of 8 days—were practically the same as those in our cases.

Orgler³² determined the uric acid elimination in two breast-fed infants aged 11 days. The average daily excretion was 41.3 and 43.3 mg., respectively, which values are somewhat greater than those obtained by us for the urine of the ninth day.

In our cases there were certain differences in the uric acid output in the two series—the early and late ligations. These are shown in Table 3.

TABLE 3.—URIC-ACID EXCRETION IN THE IMMEDIATE AND LATE LIGATION CASES

Day.	Uric Acid in Mg.			
	Average.		Per Kilo of Body Weight.	
	Immediate Ligation (4 Cases).	Late Ligation (4 Cases).	Immediate Ligation (4 Cases).	Late Ligation (4 Cases).
1	60.7	57.8	16.7	16.4
2	57.5	89.0	15.8	26.7
3	82.3	102.6	24.0	30.9
4	64.0	60.0	18.3	18.2
5	44.9	40.3	12.7	12.1
6	36.8	36.6	10.	10.5
7	35.9	36.3	9.6	10.6
8	36.7	35.3	9.7	10.
9	29.2	29.4	8.4	9.6

The most important differences occur in the values for the second and third days. For these days the average uric acid excretion and the excretion per kilo of body weight was much greater in the late ligation cases. Throughout the period of observation, with the exception of the first, fourth and fifth days, the uric acid output per kilo was greater in the late ligation cases; but the differences after the third day are slight and are not decided enough to be of significance for such a small series of cases. The average excretion after the third day is greater for some days in the immediate ligations, for others in the late ligations, but the differences are too slight to offer conclusive evidence in favor of either series.

Reusing¹⁵ observed that uric acid infarcts were less common in artificially fed infants than in those which had been nursed by their own mothers. This difference has been attributed to the greater urine excretion (from greater fluid ingestion) in the artificially fed. There is, however, another important difference. During the first two or three days of life the breast-fed infant receives colostrum which differs considerably from mature milk in both its physical and chemical characteristics. Milk is generally considered as practically purin free, and the uric acid excretion in infancy is in consequence entirely endogenous. But this applies only to the mature milk. When one considers the cellular content of colostrum as shown by microscopic examination, and the acute congestion of the breasts during the establishment of the milk secretion, it is only rational to suppose that colostrum contains an appreciable amount of

32. Orgler: *Jahrb. f. Kinderh.*, 1908, lxxvii, 383.

purin nitrogen. The results of our determinations in this connection are shown in the accompanying Table 4.

TABLE 4.—THE PURIN CONTENT OF COLOSTRUM AND THE MILK SECRETION OF THE FIRST ELEVEN DAYS

Colostrum *	Purin Nitrogen per 100 c.c. Mg.
1. Mixed specimen	3.9
2. Mixed specimen	2.99
3. Mixed specimen	3.37
4. Mixed specimen	4.07
5. Mixed specimen during acute congestion of breasts.....	5.73
6. Mixed specimen during acute congestion of breasts.....	5.9
7. Mixed specimen Case (protocol) IX, for first three days..	4.7
Milk—Mixed Specimens—	
1. First and second days of true lactation.....	2.64
2. First and second days of true lactation.....	2.49
3. Third and fourth days of true lactation.....	1.69
4. Sixth and seventh days of true lactation.....	0.57
5. Seventh and eighth days of true lactation.....	0.92
6. Tenth and eleventh days of true lactation.....	0.9
7. Case (protocol) IX, fourth, fifth and sixth days.....	1.8
8. Case (protocol) IX, seventh, eighth and ninth days.....	0.8

* We wish to acknowledge our indebtedness to Dr. Wilbur Ward, Resident Physician at Sloan Maternity Hospital, for his kindness in obtaining Specimens 3 and 5.

These results show that colostrum contains an appreciable amount of purin nitrogen, which rises to its highest value during the acute congestion of the breasts, and then gradually falls. To determine what influence the purin nitrogen of colostrum might exert on the purin excretion in the new-born, we have determined the intake of colostrum in five cases by weighing the infant before and after each nursing. In four cases the purin nitrogen was calculated from the figures shown in Table 4. In Case 9 the purin nitrogen was determined in a composite specimen of milk obtained by pumping the mother's breasts before and after each nursing. In the first four cases the purin nitrogen was determined in the feces for the period, but in Case 9 the feces were not examined for purin nitrogen owing to their use for other purposes. The usual calculations for absorption give the results shown in Table 5.

TABLE 5.—CALCULATIONS FOR ABSORPTION OF PURIN NITROGEN

	Purin Nitrogen Ingested, Mg.	Purin Nitrogen in Feces, Mg.	Purin Nitrogen Absorbed, Mg.
Case 4.	27.6	11.6	16.
Case 5.....	13.4	12.2	1.2
Case 6.....	18.3	15.3	3.
Case 7.....	23.1	18.3	4.8

Judging from these figures only a small amount of purin nitrogen is absorbed, and with the possible exception of Case 4, the quantity of uric acid from this source is negligible. A large proportion of the purin nitrogen in colostrum is probably bound in the nuclei of the colostrum corpuscles, epithelial cells and leukocytes. There is no proof that the new-born

infant is able to digest and absorb purin in these forms. There is, however, a great fallacy in the calculations for absorption. The stools of this period consist in part of meconium, which is formed in intrauterine life, and which contains a comparatively large amount of purin nitrogen. It was shown by Weintraud³³ and later by Schittenhelm³⁴ that meconium contains uric acid, which is probably derived from swallowed amniotic fluid. Meconium also contains epithelial cells which would serve as an additional source of purin nitrogen.³⁵ In our cases the first meconium stools were excluded and the feces collected after the appearance of yellowish or greenish particles, indicating a food residue. But this precaution does not eliminate the fallacy, for it is impossible to mark the exact time when the meconium stools cease and the food stools begin. Some meconium is frequently passed for from two to five days, depending on the amount of food taken.

We have no data to show that the "integral factor" of Burian and Schur—that one-half of the purin nitrogen ingested appears in the urine—applies to the new-born infant.³⁶ Assuming that this is the case, our calculations would be as shown in Table 6.

TABLE 6.—THE EXCRETION OF ENOGENOUS PURIN NITROGEN CALCULATED FROM THE PURIN NITROGEN INGESTED BY MEANS OF THE "INTEGRAL FACTOR"

	Purin Nitrogen Output During Colostral Period, Mg.	Calculated Exogenous Purin Nitrogen for the Period, Mg.
Case 4.....	90	13.8
Case 5.....	..	6.7
Case 6.....	77	9.1
Case 7.....	117	11.5
Case 9.....	94.9	5.9

The purin nitrogen ingested during the first three days can, therefore, explain but a small portion of the purin nitrogen excreted in the urine. The purin nitrogen excreted in the urine must be mainly, if not entirely, endogenous.

Purin Base Nitrogen.—The excretion of purin base nitrogen varied considerably in the individual cases but was usually most during the time of the greatest uric acid excretion. This is shown in Cases (Protocols) 1, 3, 4, 7, and 8. In Case (Protocol) 6, the amount of excreted purin base nitrogen was relatively small, while the uric acid elimination was greatest, and rose to its highest level when the uric acid was decreasing. It seems probable that the high purin base excretion and the high uric acid excretion of the former period were of the same origin, but for some

33. Weintraud: *Centralbl. f. inn. Med.*, 1895, xvi, 433.

34. Schittenhelm: *Deutsch. Arch. f. klin. Med.*, 1904, lxxxi, 423.

35. It is also true that a considerable portion of the purin nitrogen in the feces of adults does not originate from the food (Schittenhelm).

36. In experiments on infants more than 5 days of age, Nieman (see Note 31) found that the portion of the ingested purin nitrogen which was excreted in the urine was practically the same as in adults. It does not necessarily follow, however, that these experiments apply to the new-born infant.

unknown reason the excretion of the former was delayed. An indication of this delayed excretion is seen in Case (Protocol) 1, in which the highest uric acid and purin base values were not coincident. The purin bases showed only a slight increase at the time the uric acid was highest, but rose to their greatest values on the following days—times when the uric acid was decreasing. In Case (Protocol) 2 the excreted purin base nitrogen was comparatively small in amount during the entire period of observation, with the exception of a slight increase on the fourth day. The relation of the excretion of the purin bases to the uric acid excretion is shown in the new-born infant observed by Nieman;³¹ there was a great increase in the purin base excretion when the uric acid values were increasing.

The average purin base excretion in our cases is shown in Table 7.

TABLE 7.—AVERAGE EXCRETION OF PURIN BASE NITROGEN (EIGHT CASES) *

Day.	Average Excretion in Mg. All Cases.	Average Excretion in Mg. for Immediate Ligations (4 Cases).	Average Excretion in Mg. for Late Ligations (4 Cases).
1	5.3	5.2	5.5
2	9.3	7.9	10.8
3	8.1	6.5	9.7
4	6.9	6.9	7.0
5	6.1	7.3	5.1
6	5.6	4.0	7.2
7	3.7	3.3	4.0
8	3.5	3.5	3.4

* It is possible that these average figures do not indicate the true average quantities of purin base nitrogen, since the same method of estimation was not used in all cases. The variation was necessitated by the different and at times small quantities of urine available for this examination. This applies especially to Cases 1 and 2, in which the purin base nitrogen was determined in small quantities of urine. The results of the daily determinations in Cases 3 and 4 and the determinations for three-day periods in Cases 6, 7 and 8, are comparable, since the same methods were employed, with the use of approximately the same amounts of material.

Leukocytosis.—Soon after birth there is a great increase in the number of leukocytes and later a pronounced decrease. This has been shown by Gundobin,³⁷ Schiff,³⁸ and others. The average leukocyte count in our cases is shown in Table 8.

These figures show the high leukocyte count, and later, the great decrease of the leukocytes, during the first three days of life. In most instances our data are based on a single daily estimation, and therefore do not show the rather frequent fluctuation of the leukocytes during the first days of life. We cannot lay much stress on the differences shown between the immediate and late ligation cases as indicating the usual

37. Gundobin: *Jahrb. f. Kinderh.*, 1893, xxxv, 187.

38. Schiff: *Ztschr. f. Heilk.*, Prague, 1890, xi, 17; *Jahrb. f. Kinderh.*, 1892, xxxiv, 169.

conditions, for our series of cases is too small. Moreover, a single count each day is not sufficient for this purpose, but counts should be made at frequent intervals. Our results are merely intended to show the leukocyte count in the cases used in this investigation.

TABLE 8.—AVERAGE LEUKOCYTE COUNT FOR THE FIRST EIGHT DAYS (EIGHT CASES)

Day.	Leukocytes per Cubic mm. of Blood.		
	Average, All Cases.	Average, Immediate Li- gations (4 Cases).	Average, Late Ligations (4 Cases).
1	29,000	28,600	29,400
2	16,800	17,900	15,700
3	11,800	13,700	9,900
4	10,300	10,800	9,800
5	10,600	10,200	11,100
6	11,700	11,100	12,300
7	12,000	10,200	13,900
8	11,600	11,300	12,000

Total Nitrogen.—The total nitrogen excretion in our cases agreed in general with the results of other observers, but as the quantity of nitrogen was not determined in the food of most of our cases, the total nitrogen values have no special significance. There was usually a rise in the excretion of total nitrogen during the third day, coincident with the greater uric acid excretion. But it was usually on this day that the secretion of the mother's milk began, and in consequence there was a greater nitrogen intake. After the third day the total nitrogen excretion was remarkably constant. In Case 9 (Protocol IX) the nitrogen balance was determined for three day periods.³⁹ The data are given in Table 9.

In Case 4 (Protocol IV) the nitrogen balance was determined for the first three days, with the following results:⁴⁰

Milligrams of nitrogen ingested, 2,870; milligrams of nitrogen in urine and feces, 1,418; balance, +1,452=50.5 per cent. of the nitrogen ingested.

During the first three days there was a nitrogen retention in both infants in spite of the loss of weight during this period. Both infants, however, began to gain weight on the first day of the following period. The three infants observed by Langstein and Nieman⁴¹ showed a nitrogen

39. The periods in this case were exactly 72 hours each. The food nitrogen was determined from a composite specimen of milk obtained by pumping the breasts before and after each nursing. There was very little colostrum in the breasts until the end of the second day. There were two feedings during the first day; subsequently the infant was nursed at three-hour intervals. The milk secretion began on the evening of the third day.

40. The period in this case was eighty-five hours. The determination of the food nitrogen and the technic of nursing was the same as in Case 9. There was a moderate amount of colostrum in the breasts. The milk secretion began about fifty-six hours post-partum, so that the infant's food during what is recorded as the third day (see Protocol IV), consisted, in part, of the first milk secretion.

41. Langstein and Nieman: *Jahrb. f. Kinderh.*, 1910, lxxi, 604.

loss during the first three days. These infants, however, were not nursed by their own mothers but were fed on milk which had been pumped from wet-nurses.⁴² Our patients ingested much more nitrogen during this period, since they received colostrum, which is much richer in nitrogen than mature milk.⁴³

TABLE 9.—NITROGEN BALANCE IN CASE 9 DURING THE FIRST NINE DAYS OF LIFE

Period	Nitrogen Ingested Mg.	Nitrogen in Urine and Feces, Mg.	Balance Weight Mg.	Per cent. of Nitrogen Ingested
1	1,512	1,118	+394	= 26.
2	2,883	1,065	+1,818	= 63.
3	2,783	1,059	+1,724	= 61.9

During the second and third periods—from the fourth to the ninth days inclusive—there was a greater retention of nitrogen by Case 9 than by the cases of Langstein and Nieman. In one of their cases there was a nitrogen loss for the fourth and fifth days; in a second there was a negative balance for the sixth, seventh and eighth days. Michel⁴⁴ determined the nitrogen balance in one infant of four days, two of five days and one of seven days of age. The retention of the ingested nitrogen was 73 per cent., 75.7 per cent., 77.2 per cent., and 80 per cent., respectively. This higher nitrogen retention in Michel's cases was mainly due to the greater intake of nitrogen than in our case.

TABLE 10.—COMPARISON OF THE AVERAGE EXCRETION OF TOTAL NITROGEN TO TOTAL PURIN NITROGEN

Day	———Immediate Ligation——— (4 Cases).			———Late Ligation——— (5 Cases).		
	Total Nitrogen, Mg.	Purin Nitrogen, Mg.	Ratio P.N.:T.N.,	Total Nitrogen, Mg.	Purin Nitrogen, Mg.	Ratio P.N.:T.N.,
1.	197	25.4	1:7	172	24.7	1:7
2.	224	27.0	1:8	241	40.4	1:6
3.	249	33.9	1:7	332	43.9	1:7
4.	299	28.2	1:10	271	27.0	1:10
5.	294	22.2	1:13	327	18.5	1:17
6.	310	16.2	1:19	342	19.0	1:18
7.	344	15.2	1:22	274	16.1	1:17
8.	324	15.7	1:20	333	15.1	1:22

Phosphorus.—There have been only a few observations on the phosphorus excretion in the new-born, and these have given divergent results. Hecker⁴⁵ in an infant of 3 months, and Harley⁴⁶ in one of 6 months, found only traces of phosphorus. Martin and Ruge⁵ and Parrot and

42. This insured a more accurate control of the quantity and composition of the food.

43. Langstein and Nieman point out the fact that their patients received a food poorer in nitrogen than they would if they had been nursed by their own mothers and had received colostrum, instead of a more mature milk.

44. Michel: Quoted by Keller, Arch. f. Kinderh., 1900, xxiv, 1; Czerny and Keller. 289 and 294.

45. Hecker: Virchow's Arch. f. path. Anat., 1857, xi, 217.

46. Harley: Quoted by Cruse (see note 29).

Robin⁶ comment on the small phosphorus content of the urine of new-born infants. Cruse²⁹ states that phosphorus may be present only in traces in the urine of the new-born, or may be entirely absent. In his observations on the excretion of phosphates (uranium acetate titration) Cruse found from 0.008 to 0.039 per cent. in the urine of infants of 5 to 10 days of age, 0.010 to 0.058 per cent. in the urine of infants of 10 to 30 days, and 0.015 to 0.032 per cent. in the urine of infants 30 to 60 days of age. In one of the patients 5 days of age studied by Michel,⁴⁴ the average daily excretion of phosphorus was 22 mg. of P_2O_5 during a three-day period; a second infant 5 days of age excreted an average of 25 mg. of P_2O_5 a day during a four-day period. An infant of 7 days excreted a daily average of 34 mg. of P_2O_5 during a six-day period.

Moll⁴⁷ has recently emphasized the clinical importance of an estimation of the urinary phosphates. He states that the urine of a normal, thriving, breast-fed infant contains from 10 to 20 mg. of P_2O_5 a day, which type of urine he regards as being practically phosphorus-free, and 10 c.c. of which requires only a few drops of uranium acetate solution for the complete precipitation of the contained P_2O_5 . It was observed that hunger had no effect on the phosphate elimination, but that there was a greatly increased elimination during "alimentary intoxication" (Finkelstein).

It was noted in our earlier cases in which the phosphorus was not determined (Protocols I, II, III and IV), that during the first few days the addition of the uranium acetate reagent of Folin and Shaffer produced a well-defined precipitate of uranium phosphate. During the later days the addition of this reagent produced, at most, a faint cloud and never a distinct precipitate. The total phosphorus was determined in four cases during three-day periods. The results are given in Table 11.

TABLE 11.—THE EXCRETION OF TOTAL PHOSPHORUS IN THE URINE OF CASES 6, 7, 8. AND 9. DURING THREE-DAY PERIODS

Case	P_2O_5 in Mg.				Average
	6	7	8	9	
Period 1. . . .	46	44	63.4	60.7	53.5
Period 2. . . .	Trace*	Trace*	Trace*	25.6	6.4
Period 3. . . .	Trace*	4.2	11.8	27.2	10.8

*Gave a distinct precipitate of ammonium phospho-molybdate but the magnesium pyrophosphate precipitate was too small to weigh with accuracy. The phosphorus determinations were always made from as large a quantity of urine as possible; usually from one-fourth to one-half of the total urine for the period.

In Case 6 a daily determination was made after the third day. In Case 7 the phosphorus was determined in a composite specimen for the first three days, and for the seventh, eighth and ninth days, while a daily determination was made during the fourth, fifth and sixth days. In Cases 8 and 9 the phosphorus was determined in composite specimens for three-day periods. In Case 5 the urine of the second day was incomplete

47. Moll: *Jahrb. f. Kinderh.*, 1909, lxi, 128.

and the phosphorus was determined in the composite specimen for the first and third, and the fourth and fifth days. The urinary phosphorus was as great during the fourth and fifth as during the first and third days. During the last day of observation the infant began to vomit and to suffer from a severe, watery diarrhea. This high phosphorus output on the fourth and fifth days is in marked contrast with the results in the other cases. This discrepancy may have been caused by an increased elimination of phosphorus, due to the gastro-intestinal disorder in harmony with Moll's view.

Langstein and Nieman⁴¹ have determined the phosphorus elimination in three new-born infants, but their results differ considerably from ours. Their cases did not show a greater phosphorus elimination during the first three days, but on the contrary, the excretion usually increased after this time.

In Case 9 (Protocol IX) the phosphorus balance was determined. The results are given in Table 12.

TABLE 12.—THE PHOSPHORUS BALANCE IN CASE 9 DURING THREE-DAY PERIODS *

Period	P ₂ O ₅ Ingested, Mg.	P ₂ O ₅ in Urine and Feces, Mg.	Balance Weight, Mg.	Per cent. of P ₂ O ₅ Ingested
1.	155.5	85.5	+ 70.	= 45.0
2.	492.9	67.9	+425.	= 86.2
3.	483.	88.8	+394.2	= 81.6

*The phosphorus content of the food was determined from a composite specimen of milk obtained by pumping the breasts before and after each nursing.

The percentage of phosphorus retained in this case closely corresponds with the results in Michel's⁴⁴ cases. Two infants of 5 days retained 87.3 and 77.3 per cent. of the phosphorus (P₂O₅) ingested; an infant of 7 days retained 80.1 per cent. of the phosphorus intake.

Acidity.—The acidity of the urine was determined in Case 8 by the method of Folin. Both the absolute and the percentage acidity were greatest during the first three days. The highest percentage acidity was on the second day, the greatest absolute acidity on the third day.

III. GENERAL CONSIDERATION OF THE URIC ACID EXCRETION AND THE CAUSATION OF THE URIC ACID INFARCTS

The results of Reusing, Sjöqvist and ourselves show that there is a comparatively abundant output of uric acid from the new-born. Those of Sjöqvist and ourselves show that this excretion is greatest during the period in which post-mortem examination and the occurrence of infarct elements in the urine indicate that uric acid is deposited in the kidney tubules. There are two possible explanations for the high uric acid output in the new-born: (1) a normal uric acid formation and a diminished destruction, or (2) increased formation with normal or diminished destruction.

Spiegelberg⁴⁸ found that when 0.1 gm. of uric acid per kilo of body weight was injected into young puppies, 53 per cent. was excreted in the urine, while in adult animals only 5.6 per cent. of the injected uric acid could be thus recovered. He was able to produce deposits of uric acid in the kidneys of puppies by the injection of quantities which were without effect on the older animals. He further observed that, after the uric acid injections, the urine of the puppies became cloudy, while that of the older animals remained clear. These experiments indicated that the young animals were less able to destroy uric acid than were the adults, and suggested that a deficient uric acid destruction was perhaps the explanation of the high excretion in the new-born. This explanation was supported by the studies of Mendel and Mitchell,⁴⁹ who observed that the uricolytic enzyme was the last to appear in the developing pig. Observations on the human organism, however, gave different results. Schittenhelm and Schmid⁵⁰ were able to show an active uricolysis by the organs of the fetus and the new-born infant. These results are of particular interest in contrast with the results of Schittenhelm,⁵¹ and Künzel and Schittenhelm,⁵² who were unable to demonstrate the presence of a uricolytic enzyme in the organs of adults. Wells and Corper⁵³ found no evidence of uricolytic activity in the organs of the fetus, the new born, or in those of adults. They therefore concluded that the human organism does not possess the ability to destroy uric acid. The results of Wiechowski⁵⁴ have a similar bearing, for he was able to recover in the urine a considerable portion of the uric acid injected into human beings (60 to 80 per cent.). Moreover, he was unable to demonstrate the presence of allantoin in the urine after the uric acid injections.

It seems, therefore, that the results of Spiegelberg on dogs are not applicable to the human organism. This variation is perhaps due to the fact that dogs normally have the power of destroying uric acid.

The second hypothesis—an increased uric acid formation—is favored by Reusing¹⁵ and by Flensberg.¹⁰ As shown by Gundobin,³⁷ Schiff³⁸ and others, soon after birth there is a rapid rise in the number of the leukocytes, which later shows a pronounced fall. The high uric acid formation was thus explained on the basis of Horbaczewski's theory.

The relationship of the leukocytes in the peripheral blood to the elimination of uric acid is a problem on which there is an enormous controversial literature, and which at the present time remains unsolved. There is little doubt that uric acid can arise from the nuclein of leukocytes, as

48. Spiegelberg: *Arch. f. exper. Path. u. Pharmakol.*, 1898, xli, 428.

49. Mendel and Mitchell: *Am. Jour. Physiol.*, 1907, xx, 97.

50. Schittenhelm and Schmid: *Ztschr. f. exper. Path. u. Therap.*, 1907, iv, 424.

51. Schittenhelm: *Ztschr. f. Physiol. Chem.*, 1909, lxi, 248.

52. Künzel and Schittenhelm: *Zentralbl. f. Physiol. u. Path. d. Stoffwech.*, 1908, iii, 721.

53. Wells and Corper: *Jour. Biol. Chem.*, 1909, vi, 321.

54. Wiechowski: *Arch. f. exper. Path. u. Pharmakol.*, 1909, lx, 185.

well as from the nuclein of other tissues. The observations of Fränkel,⁵⁵ Jakob,⁵⁶ Jakob and Krüger⁵⁷ and Musser and Edsall⁵⁸ in leukemia and of Kühnau⁵⁹ and others in pneumonia, gives evidence of the origin of uric acid from leukocytes. We have no evidence to show, however, that the number of leukocytes in the peripheral blood is an accurate index of the total number of these cells, nor that a decrease in the leukocyte count means a leukocyte destruction. It has been demonstrated by Goldscheider and Jacob,⁶⁰ Schulz,⁶¹ Bohland⁶² and others that a decreased number of leukocytes in the peripheral blood may only mean a changed distribution of these cells. These observers showed that when such a decrease was induced experimentally in animals, it was compensated by an accumulation of the leukocytes in the lung capillaries. In other words, these experiments indicate that fluctuations of the leukocyte count do not necessarily signify changes in the total number of these cells, but may merely indicate altered proportions in the peripheral circulation and the internal organs.

The apparent relationship of the leukocyte count to the uric acid excretion is shown by the tabulated data for our cases. There was usually an inverse ratio between the leukocyte count and the uric acid elimination during the first four days. There was a great decrease in the leukocyte value during the period when the uric acid figures were largest, which coincides with the time when the uric acid infarcts occur. The excretion of phosphorus followed a similar course; it was high during the first three days and then fell sharply to quantities which were often too small to estimate. It is well known that nuclear material is rich in phosphorus as well as in the precursors of uric acid, and this parallelism in the excretion of uric acid and phosphorus strongly suggests that their joint origin is from cell nuclei. It therefore seems correct to attribute the augmented uric acid excretion to an increased formation of that substance.

A more difficult problem arises when we attempt to determine whether this uric acid originates from leukocytolysis or finds its origin in other tissues. The high uric acid excretion occurs at a period when the blood is undergoing rapid morphologic changes. During fetal life and shortly after birth many of the red cells contain nuclei which disappear during the first few days of life. Shortly after birth the leukocytic formula shows a predominance of the polynuclear neutrophilic cells, but within

55. Fränkel: *Deutsch. med. Wehnschr.*, 1895, xxi, 639.

56. Jakob: *Arch. f. Physiol. u. Anat. (Dubois-Reymond)*, *Physiol. Abth.*, 1894, 378.

57. Jakob and Krüger: *Deutsch. med. Wehnschr.*, 1894, xx, 641.

58. Musser and Edsall: *Univ. Penn. Med. Bull.*, 1905, xviii, 174.

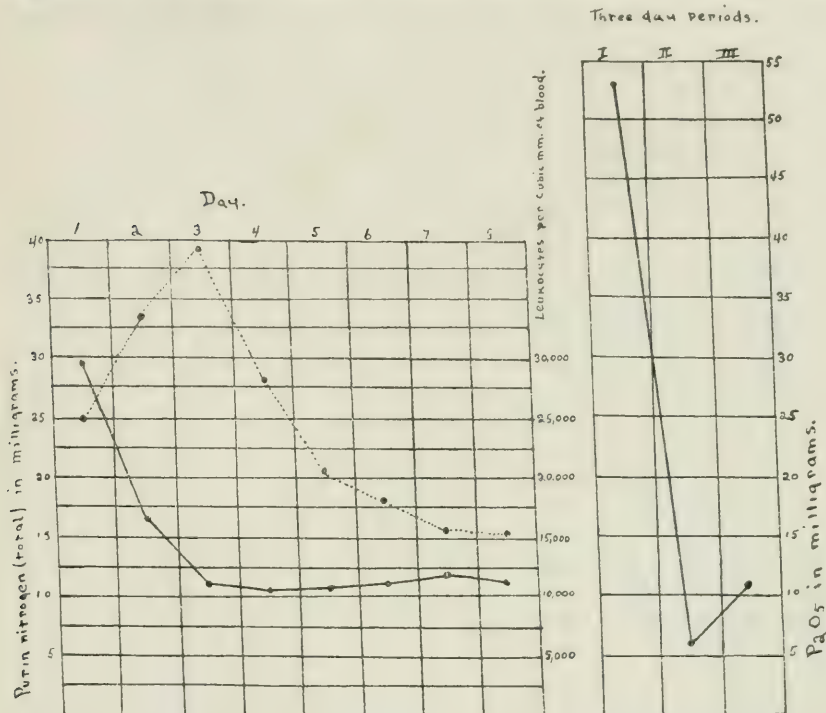
59. Kühnau: *Ztschr. f. klin. Med.*, 1897, xxxii, 482; *Deutsch. Arch. f. klin. Med.*, 1897, lviii, 339.

60. Goldscheider and Jacob: *Ztschr. f. klin. Med.*, 1894, xeviii, 373.

61. Schultz: *Deutsch. Arch. f. klin. Med.*, 1893, li, 234.

62. Bohland: *Centralbl. f. inn. Med.*, 1899, xx, 361.

a few days the proportion changes and the typical infantile blood picture—a predominance of lymphocytes—is apparent (Carstanjen⁶³). There is at first an increase in the number of leukocytes in the peripheral blood, and later a pronounced decrease. It has been mentioned that when the new-born infant is left attached to the placenta some time after birth it receives a much larger amount of blood than when the umbilical cord is ligated immediately after birth. If the uric acid arises from the morphologic elements of the blood, it is to be expected that the excretion would be greater in the cases in which the umbilical cord was tied late.⁶⁴ That



Curve 1.—Comparison of the leukocytosis with the excretion of P_2O_5 and total purin nitrogen. Leukocytes, continuous line; total purin nitrogen, dotted line. The data for the purin nitrogen and leukocytes were obtained from all of the cases.

63. Carstanjen: *Jahrb. f. Kinderh.*, 1900, liii, 215.

64. Reusing has suggested that the uric acid output should be greater in late ligation cases if the increased excretion of that substance in the new born originated from leukocytolysis; but he apparently made no observations bearing on this problem. The work of Hofmeier and Silvermann indicates that there is a destruction of the blood elements in icterus neonatorum. On the basis of this observation, Reusing has suggested that if the uric acid originates from a destruction of blood cells, there should be a greater excretion of uric acid by jaundiced infants. The two cases observed by Reusing give no conclusive evidence on this point. Two of our cases (Protocols IV and VII) developed a mild grade of icterus neonatorum. The degree of jaundice was very slight, however, and was evidenced only by a faint yellow color of the conjunctiva. In neither case was the excretion of uric acid greater than in the infants without jaundice.

this is the case is shown by the results from our cases. During the second and third days the average uric acid excretion, and the excretion in relation to the body weight, were greater in the late ligation cases. These observations would seem to indicate that the blood elements are in some way concerned with the increased uric acid formation in the new born. The pronounced decrease in the leukocyte count, and the disappearance of a great number of polynuclear cells from the peripheral blood, suggests that the uric acid arises from a leukocyte destruction. Although this evidence is suggestive, there is no proof that these changes signify a leukocyte destruction, and it is impossible to determine whether the uric acid arises wholly, or in part, from an increased number or an increased destruction of leukocytes, or from the extruded nuclei of the red cells. Perhaps it originates in some phase of metabolism concerned with the *production* of the formed elements of the blood.

The exciting cause for the deposition of uric acid in the kidney tubules is not entirely clear. We found that the acidity of the urine was greatest during the first three days, which is coincident with the formation of the infarcts. This high acidity of the urine may be a factor in causing the deposition of uric acid, for uric acid is readily thrown out of solution by increased acidity of the urine.

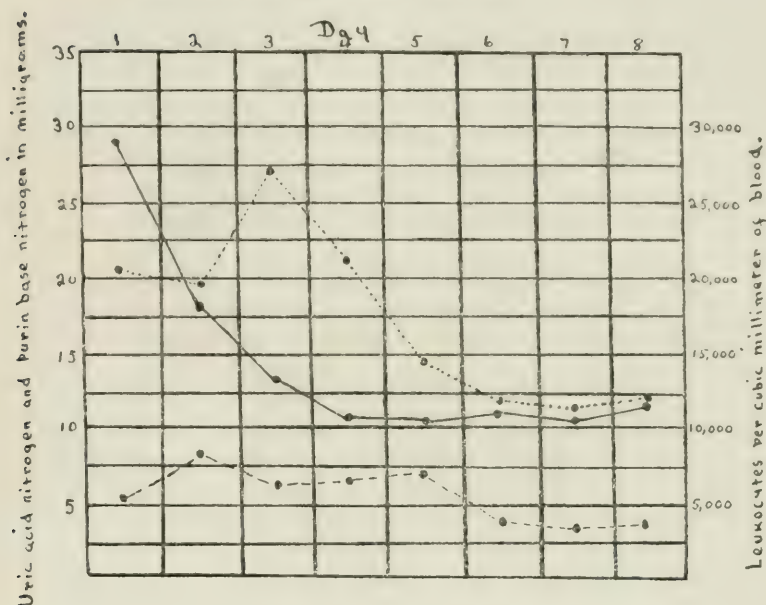
Any acceptable hypothesis must explain not only the deposit of the uric acid in the kidney but also the formation of the infarct elements and stroma. The uric acid is not deposited directly in the kidney tubules but is found in the characteristic cylinders and spheres. There are certain objections to Ebstein's hypothesis—the primary deposit of uric acid and a secondary formation of the infarct stroma through cell necrosis. Spiegelberg has shown that the urine of the new-born infant has great solvent powers for uric acid, and that urine which was turbid with urates was still able to dissolve considerable quantities. It is also well known that the urine of adults may contain very large amounts of uric acid; yet uric acid infarcts never occur in adult life.

The explanation of Flensberg was based on careful histologic examination of the kidney of the fetus and the new-born infant. He showed the presence of the cylinders in the kidney tubules before the occurrence of the infarcts. It remains to be determined whether the contact of these cylinders with the concentrated and highly acid urine is sufficient to excite a deposit of uric acid on their surface, or whether the deposition of the uric acid depends on some special physical or chemical characteristic of the urine.

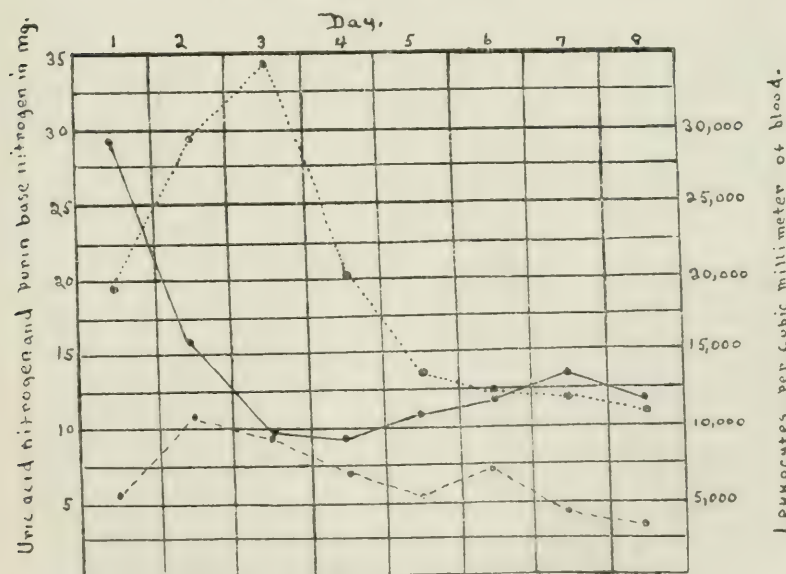
IV. SUMMARY AND CONCLUSIONS

1. Uric acid infarct elements were present in the urine of each of nine new-born infants.

Immediate ligation of cord.



Late ligation of cord.



Curve 2.—Relation of the number of leukocytes (continuous line) to the elimination of uric acid nitrogen (dotted line) and purin base nitrogen (broken line).

2. (a) The uric acid output in new-born infants is both absolutely and relatively high. It is greatest during the first three days and then decreases.

(b). In cases in which the umbilical cord was ligated late, the output of uric acid was greater during the second and third days than in cases in which the cord was ligated immediately after birth.

(c). The quantity of the purin substances in the colostrum ingested is too small to explain the observed high uric acid output.

3. The total phosphorus excretion was high during the first three days and then showed a sharp diminution. There is marked retention of phosphorus by the new-born infant.

4. There is a moderate nitrogen retention during the first three days of life. Later, nitrogen is retained in large degree.

5. There is an inverse ratio between the leukocyte count and the elimination of phosphorus and uric acid during the first few days of life.

6. In the light of our present knowledge, the parallelism between the excretion of uric acid and phosphorus during the first three days would seem to indicate a common origin from cell nuclei. The greater excretion of uric acid in the late ligation cases suggests that the formed elements of the blood in some way serve as its origin.⁶⁵

We desire to thank Professor Gies for his kindness in placing the facilities of his laboratories at our disposal, and to acknowledge our great indebtedness to him and his associate, Dr. J. Rosenbloom, for much valuable assistance. We wish also to acknowledge our indebtedness to Dr. Rowland G. Freeman for permitting us to use the material from his service at the New York Nursery and Child's Hospital, and to thank the superintendent and nurses for their cooperation. We are also greatly indebted to Mr. F. W. Shaffer for much assistance in the supervision of the cases from the Nursery and Child's Hospital, and to Miss R. Feagin for her careful supervision of Case 9.

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65. In addition to the numbered references the following have been freely consulted:

Hall: *The Purin Bodies*, 1904.

Hill: *Recent Contributions to Physiology and Biochemistry*, 1906.

Wiener: *Ergebnisse der Physiologie*, 1902, i, 555; 1903, ii, 377.

McCrudden: *The Chemistry, Physiology and Pathology of Uric Acid*, 1905.

Barker: *Truth and Poetry Concerning Uric Acid*, 1905.

Mendel: *Harvey Lecture*, 1905-1906, *Jour. Am. Med. Assn.*, 1906, xlii, 842 and 944.

Lusk: *The Science of Nutrition*, 1909.

PROTOCOL I.—CASE 1.—IMMEDIATE LIGATION OF UMBILICAL CORD, FIRST CHILD

Day	Weight, Gm.	Specific Gravity	Quantity c.c.	Urine			Leukocytes per c.mm. of Blood
				Uric Acid Mg.	Purin* Base Ni- trogen, Mg.	Total Nitrogen, Mg.	
1. 38 hours	3,642	1014	32	43.	2.3	136.	28,100
2.	3,494	1018	25	23.8	2.3	148.2	14,000
3.	3,494	1011	130	101.6	4.7	269.4	17,400
4.	3,614	1004	280	98.5	12.9	243.1	14,200
5.	3,676	1005	350	75.2	12.9	199.6	12,700
6.	3,616	1005	290	45.3	4.5	284.1	8,000
7.	3,676	1004	290	43.8	6.5	310.	11,700
8.	3,676	1004	360	50.6	4.9	308.1	11,000

*Daily determination by Kenneway's modification of the Cammerer-Arnstein method.

PROTOCOL II.—CASE 2.—LATE LIGATION OF UMBILICAL CORD. SECOND CHILD

Day	Weight, Gm.	Specific Gravity	Quantity c.c.	Urine			Leukocytes per c.mm. of Blood
				Uric Acid Mg.	Purin* Base Ni- trogen, Mg.	Total Ni- trogen, Mg.	
1. 25 hours	3,568	1016	30	47.5	3.7	127.6	24,500
2.	3,269	1010	32	76.5	2.7	142.	14,300
3.	3,227	1010	part lost				7,300
4.	3,269	1007	310	77.5	7.1	220.	7,600
5.	3,227	1005	310	53.7	1.4	310.8	7,500
6.	3,255	1005	part lost				12,600
7.	3,295	1005	268	50.	4.3	196.4	13,200
8.			...				11,400

*Daily determination by Kenneway's modification of the Cammerer-Arnstein method.

PROTOCOL III.—CASE 3.—LATE LIGATION OF UMBILICAL CORD. FIRST CHILD

Day	Weight, Gm.	Specific Gravity	Quantity c.c.	Urine			Leukocytes per c.mm. of Blood
				Uric Acid Mg.	Total* Purin Ni- trogen, Mg.	Total Ni- trogen, Mg.	
1. 24 hours	3,479	1020	12	37.8		169.4	38,000
2.	3,367	1012	110	142.5	73.8	342.1	15,800
3.	3,367	1007	210	104.16	49.7	326.2	11,600
4.	3,339	1005	280	56.6	22.6	266.5	11,000
5.	3,425	1005	370	37.	14.3	355.8	14,000
6.	3,425	1007	365	42.8	18.5	347.4	14,400
7.	3,507	1005	275	31.	14.1	261.8	17,900
8.	3,624	1004	390	29.9	12.2	371.2	13,700

*Daily determination by the method of Krüger and Schmid.

PROTOCOL IV.—CASE 4.—IMMEDIATE LIGATION OF UMBILICAL CORD. SECOND
CHILD. VERY SLIGHT DEGREE OF ICTERUS NEONATORUM

Day	Weight, Gm.	Food				Urine				Feces				Leukocytes per c.mm. of Blood
		Quantity, Gm.	Purin Ni- trogen, Mg.	Total Ni- trogen, Mg.	Specific Gravity	Quantity c.c.	Uric Acid, Mg.	Total* Purin Nitrogen, Mg.	Total Ni- trogen, Mg.	Total Nitrogen, Mg.	Purin Nitrogen, Mg.	Nitrogen Mg.	Nitrogen Mg.	
1. 37 hours	4,200	135.			1012	72	62.7	23.2	295.4					21,000 32,000
2.	4,050	291.5			1020	43	86.3	39.1	294.1					
3.	3,900	310.			1009	112	72.	27.7	286.					12,100
For period			27.6	2,870						543.7	11.6	+1,452		
4.	3,930				1006	249	50.5	19.1	355.4					8,700
5.	3,990				1005	415	30.4	13.8	340.6					9,800
6.	4,020				1005	450	36.0	14.0	348.3					11,000
For period										587.6	4.2			
7.	4,140				1005	410	41.	15.4	348.3					7,500
8.	4,230				1005	400	31.2	14.8	361.6					8,000
For period										141.3	6.4			

* Daily determination by the method of Krüger and Schmidt.

PROTOCOL V.—CASE 5.—IMMEDIATE LIGATION OF UMBILICAL CORD, FIRST CHILD

Day	Weight, Gm.	Food				Urine					Feces		Leukocytes per cmm. of Blood
		Quantity, Gm.	Purin Nitrogen Mg.	Specific Gravity	Quantity c.c.	Uric Acid, Mg.	Purin* Base Nitrogen, Mg.	Total Ni- trogen, Mg.	P ₂ O ₅ , Mg.	Total Ni- trogen, Mg.	Purin Ni- trogen, Mg.		
1. 25 hours	3,201	...	...	1011	28.5	28.5	...	173.8	...	...	...	{ 16,500** 26,500† 29,800‡ 21,200 15,575 7,200 8,700	
2.	3,100	120	...	1014	part lost	...	...	...	...	...	...		
3.	3,060	280	...	1011	75.	76.2	...	221.1	...	...	...		
For period	...	...	13.4	...	...	...	18.1	...	37.4	306.1	12.2		
4.	3,120	...	...	1010	92.	61.	...	312.8	...	...	...		
5.	3,150	...	...	1008	170.	40.4	...	297.2	...	...	...		
For period	...	...	...	...	...	...	specimen lost	...	36.9	192.	4.9		

*Determined in the composite specimen by Kenney's modification of the Cammerer-Arnstein method.

**Half hour after birth.

†Seven hours after birth.

‡Fourteen hours after birth.

PROTONOL VI. CASE 6. LATE LIGATION OF UMBILICAL CORD. FIRST CHILD

Day	Weight, (gm.)	Food				Urine				Feces				Leukocytes per c. mm. of Blood
		Quantity, (gm.)	Purin Nt- rogen, Mg.	Specific Gravity	Quantity, c.c.	Uric Acid, Mg.	Purin Base*, Mg.	Total Nt- rogen, Mg.	P ₂ O ₅ , Mg.	Total Nt- rogen, Mg.	Purin Nt- rogen, Mg.	Total Nt- rogen, Mg.	Purin Nt- rogen, Mg.	
1. 22 hours	3,900	20		1020	19	29.2		134.4	..					{ 17,175† 32,345§ 25,100¶
2.	3,660	190		1015	70	68.7		286.8	..					
3.	3,570	300		1009	130	105.3		360.5	..					
For period			18.3				9.3		46	918.3	15.3			
4.	3,690			1004.5	335	71.9		385.4	Trace†					10,600
5.	3,780			1004	300	30.		340.	Trace†					11,500
6.	3,870			1005	360	30.2		297.8	Trace†					11,000
For period							37.4		..					
7.	3,840			1006	400	32.6		367.6	Trace†					11,800
8.	3,885			1006	380	36.1		310.2	Trace†					11,400
For period							14.		..					

* Determined in the composite specimen by Kenneway's modification of the Cammerer-Arnstein method.

† Molybdate precipitate very light; no weighable $Mg_2P_2O_7$.

‡ Two hours after birth.

§ Seven hours after birth.

¶ Fourteen hours after birth.

PROTOCOL VII.—CASE 7.—IMMEDIATE LIGATION OF UMBILICAL CORD. FIRST
CHILD. VERY SLIGHT DEGREE OF ICTERUS NEONATORUM

Day	Weight, Gm.	Food				Urine				Feces				Leukocytes per c.mm. of Blood
		Quantity, Gm.	Purin Ni- trogen, Mg.	Specific Gravity	Quantity, c.c.	Uric Acid, Mg.	Purin* Base Nitrogen, Mg.	Total Ni- trogen, Mg.	P ₂ O ₅ , Mg.	Total Ni- trogen, Mg.	Purin Ni- trogen, Mg.			
1. 38 hours	3,479	80		1016	47	108.9		179.	..				{ 19,900½ 24,500½ 23,900½	
2.	3,367	190		1018	75	62.6		230.1	..					
3.	3,227	230		1010	114	79.5		220.6	..					
For period			23.1				33.4		44	814.8	18.3			
4.	3,255	240		1008	190	46.2		286.2	Trace†			13,100		
5.	3,255			1008	230	33.8		343.1	Trace†			9,900		
6.	3,339			1007	300	29.2		298.4	Trace†			14,300		
For period							16.7		..					
7.	3,395			1007	375	23.		386.4	..			11,600		
8.	3,395			1006	340	28.5		310.4	..			15,000		
9.	3,451			1006	375	29.2		301.2	..			17,000		
For period							4.1		42.5					

*Determined in the composite specimen by Kewenaw's modification of the Cammerer-Arnstein method.

†Slight molybdate precipitate; no weighable Mg₂P₂O₇. ‡One hour 40 minutes after birth.

§Eighteen hours after birth. §§425 c.c. of urine used for determination. ¶Twenty-four hours after birth.

PROTOCOL VIII.—CASE 8.—LATE LIGATION OF UMBILICAL CORD. FIRST CHILD

Day	Weight Gm.	Specific Gravity	Quantity, c.c.	Urine				Acidity§		
				Uric Acid, Mg.	Purin* Base, Nitrogen, Mg.	Total Nitr- rogen, Mg.	P ₂ O ₅ † Mg.	Per 100	Total	Leukocytes per c.mm. of Blood
1. 31 hrs.	3,110	1012	43	116.9		158.4		27.40	11.78	22,800
2.	3,110	1015	39	68.4		198.9		41.76	16.28	13,600
3.	2,998	10075	240	98.4		312.7		7.76	18.61	9,300
For period.	...		...		33.8		63.4			
4.	2,970	1008	182	36.2		216.5		5.24	9.53	10,000
5.	2,879	1007	222	40.6		314.5		4.96	11.01	11,600
6.	2,942	1007	270	35.9		382.5		5.24	14.14	11,500
For period	...		...		14.8		Trace‡			
7.	2,998	1007	275	31.6		374.		4.96	13.64	12,700
8.	3,044	1007	290	40.		328.8		4.96	14.38	11,600
9.	3,044	1007	320	29.4		253.7		3.54	11.32	9,700
For period	...		...		3.4		11.8			

‡Slight molybdate precipitate; No weighable Mg₃P₂O₇.

§In cubic centimeters of N/10 NaOH.

*Determined in the composite specimen by Kenneway's modification of the Cammerer-Arnstein method.

†The urine used for the determination of the acidity was afterwards used in the phosphorus determination. Since free oxalic acid interferes with the precipitation of ammonium phosphomolybdate, blank determinations were made. Duplicate phosphorus determinations were made in a solution of sodium dihydrogen phosphate with the following results:

	MAGNESIUM PYROPHOSPHATE, Gm.
1. 25 c.c. of phosphate solution	0.0395 0.0398
2. 25 c.c. of phosphate solution with the addition of nitric and sulphuric acids.....	0.0396
Not heated	0.0389
3. 25 c.c. of phosphate solution with the addition of nitric and sulphuric acids and 10 gm. of potassium oxalate	No molybdate precipitate.
Not heated.	
4. 25 c.c. of phosphate solution with the addition of nitric and sulphuric acids and 10 gm. of potassium oxalate	0.0397
Heated as in the Neuman oxidation method.....	0.0391

It is thus seen that when the Neuman method of oxidation is used, the presence of oxalic acid does not interfere with the determination.

PROTOCOL IX.—CASE 9.—LATE LIGATION OF UMBILICAL CORD. FIRST CHILD

Day	Weight Gm.	Food				Urine				Feces						
		Quantity, Gm.	Total Nt. Mg.	Purin Nt. Mg.	P ₂ O ₅ Mg.	Quantity, cc.	Specific Gravity	Total Nt. Mg.	Purin Nitrogen ² Abso- lute, Mg.	As Uric Acid, Mg.	P ₂ O ₅ Mg.	Total Nt. Mg.	P ₂ O ₅ Mg.	Nitrogen Balance Mg.	Phosphorus Balance Mg.	Leukocytes per cmm.
1. 24 hours	3,600	15				32	1013	168.3	23.8	71.4						39,000
2.	3,500	100				40	1017	146.2	29.2	87.6						26,000
3.	3,230	140				120	1017	284.	41.9	125.7						14,000
For period			1,512	11.9	155.5						60.7	520.	24.8	+ 394	+ 70	
4.	3,260	290				200	1008	310.3	26.	78.0						14,300
5.	3,260	310				220	1008	297.4	21.3	63.9						10,100
6.	3,300	330				260	1006	318.6	16.6	49.8						8,000
For period			2,883	16.7	492.9						25.6	141.1	42.3	+ 1,818	+ 425	
7.	3,390	360				280	1005	299.8	16.1	48.3						10,400
8.	3,430	360				240	1004	308.5	14.9	44.7						12,200
9.	3,520	430				300	1004	313.4	16.0	48.0						9,800
For period			2,783	8.08	483.						27.2	139.6	61.6	+ 1,724	+ 395	

*Daily determination by the method of Krüger and Schmid.

THE NON-SPECIFICITY OF THE CYTO-FINDINGS IN THE SPINAL FLUID IN VARIOUS MENINGEAL CONDITIONS, ESPECIALLY IN CHILDREN

FROM AN EXAMINATION OF OVER FIVE HUNDRED SPECIMENS

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Text-books which deal with the examination of the spinal fluid give much space to elaborate schemes for a positive diagnosis from the spinal fluids in the different forms of meningitis. However, if one has had these same spinal fluids to examine, one is immediately impressed with the fact that no absolute rules will hold. This is especially true in cases of suspected tuberculous meningitis. Several recent articles have claimed a cure in cases of tuberculous meningitis, the diagnosis of which has been based on the mere counting of the cells, and a differential study of these cells.

In direct opposition to this point of view it may be interesting to note the findings in several different conditions, that have come under observation, which commonly occur in children.

The diagnosis of epidemic meningococcus meningitis is never based solely on the finding of an excess of polynuclears in the exudate. The infecting organism is the most important finding, and on it is based not only the treatment, but also the prognosis.

Nor is one justified in diagnosing a case as one of tuberculous meningitis because the fluid contains a preponderance of mononuclear cells, or lymphocytes. The etiologic causes underlying these findings are, to be sure, very much harder to determine than in the instance of fluids in which the organism is easily discoverable, and almost as easily identified. But even in long continued pyogenic infections in which the process has become chronic, the reversion from a polynuclear to a mononuclear predominance is seen. Just why this reaction should occur may not be perfectly clear, but still it remains a fact that in this respect the reaction of the meninges resembles that of the true serous membranes, pleural, pericardial and peritoneal, and even the synovial membranes.

All these membranes react in a more or less parallel and uniform way to various infecting agents. Each membrane is, of course, governed by certain definite, normal conditions. Understanding and realizing these normal limits and conditions is essential in understanding the reactions to certain infectious agents. The reason why certain infectious

agents act as they do on these different membranes is not nearly so clear. The exact reasons for these chemotactic properties depend, undoubtedly, on certain factors in protective immunity, of which as yet little is known. It is true of all this group of membranes that the pyogenic organisms at first exert a polynuclear chemotaxis, and if they become chronic, a mononuclear chemotaxis replaces the original polynuclear one.

It is equally true that certain other organisms (*Spirochæta pallida*, tubercle bacillus) and certain toxins and viruses (toxins of almost any pyogenic organism, e. g., pneumococcus, see Cases 1, 7 and 8, Table 3; the virus of rabies and epidemic myelo-encephalitis [anterior poliomyelitis]) produce a mononuclear, or lymphocytic chemotaxis. It is quite as erroneous to pronounce a diagnosis of tuberculous meningitis from the cytologic picture of a mononuclear predominance in the fluid, as it would be to pronounce a case meningococcus meningitis from the polynuclear excess. True, in both cases, due to the predominance of these two types of infection, one might be right in his diagnosis, and still be working in the realm of guess-work.

In an earlier article¹ attention was called to the occurrence of encephalitis in children, and also to the fact that the findings in the spinal fluid in such cases were identical in many cases with those found in tuberculous meningitis. The spinal fluid in such cases was identical in many cases with that found in tuberculous meningitis. The spinal fluid in encephalitis is increased in amount and is under pressure, and may be opalescent, or even slightly turbid from the excess of cells found in the fluid, which are mainly of the mononuclear and lymphocytic type.

Table 1, showing cases of encephalitis, from the Children's Hospital, occurring during the past four years, will perhaps make these points more clear. To this class probably belong the majority of cases of mistaken diagnosis.

The recent studies in epidemic myelo-encephalitis (anterior poliomyelitis) by Flexner and Lewis, in this country, have brought this epidemic disease very prominently before the medical profession. In an attempt to get some points in the early diagnosis of this condition I have been able to show both by experimental means,² in spinal fluids from monkeys, and from the spinal fluid in eleven cases of undoubted, and several cases of abortive, myelo-encephalitis in children, the occurrence in the spinal fluid of large numbers of mononuclear cells, or

1. Southard, E. E., and Lucas, William P.: Encephalitis in Children, with Reference to Frequency of Epilepsy following Recovery. (Unpublished.)

2. Lucas, W. P.: The Diagnosis of Infantile Paralysis in the Prodromal and Early Acute Stage as Found in the Experimental Study of Acute Poliomyelitis in Monkeys, with Reports of Findings in Four Human Cases. *Boston Med and Surg. Jour.*, 1910, clxiii, 245; Gay, Frederick P., and Lucas, William P.: Anterior Poliomyelitis, Methods of Diagnosis from Spinal Fluid and Blood in Monkeys and Human Beings. *Arch Int. Med.*, 1910, vi, 330.

TABLE 1.—AGE, ONSET, PHYSICAL SIGNS AND FINDINGS IN THE CEREBROSPINAL FLUID IN TWELVE CASES OF ENCEPHALITIS

Case No.	Age	Onset	Nervous Symptoms	Reflexes	Amount c.c.	Pressure	Character	Clot Formation	Cell Count per c.mm.	Differential
1	2 yrs.	Sudden.	Convulsions.	Kernig on left side; rigidity of neck.	30	Moderate.	Slightly opalescent.	Fine clot.	100	Mononuclears in excess.
2	6½ yrs.	Gradual.	Stupor.	Ptoxis of right eyelid.	40	Moderate.	Clear.	Fine clot; fibrin shreds.	50	Lymphocytes.
3	4 yrs.	Gradual.	Convulsions.	Kernig sign present; aphasia.	20	Slight.	Clear.	Fine clot.	80	Mononuclears 80 %.
4	3 yrs.	Gradual.	Stupor.	Rigidity of neck.	10th day, 30	Moderate.	Opalescent.	Moderate.	120	Polynuclears 55 %.
5	2½ yrs.	Sudden.	Dull.	Neck sign present.	19th day, 25	Moderate.	Opalescent.	Slight.	160	Mononuclears 45 %.
6	4 yrs.	Sudden.	Dull.	Neck rigid; neck sign present.	35	Moderate.	Clear.	None.	10	All mononuclears.
7	2 yrs.	Sudden.	Delirious.	Photophobia; neck sign and Kernig present.	45	Marked.	Clear.	Spider-web clot.	20	Polys. and monos. equal.
8	4 yrs.	Sudden.	Convulsions.	Strabismus; choked disk.	30	Moderate.	Opalescent.	Spider-web.	480	Mononuclears 97 %.
9	3 yrs.	Sudden.	Convulsions.	Rigidity of neck; facial paralysis; strabismus.	25	Moderate.	Opalescent.	Slight.	185	Mononuclears 85 %.
10	5 yrs.	Sudden.	Marked pain.	Rigidity of neck; strabismus.	40	Marked.	Slightly opalescent.	Moderate.	82	Mononuclears 95 %.
11	4 yrs.	Slow.	Sensitive.	Absent.	25	Moderate.	Opalescent.	Moderate.	200	Lymphocytes 100 %.
12	1 yr.	Sudden.	Convulsions.	Absent; pupils unequal and sluggish.	50	Marked.	Clear.	None.	25	Lymphocytes 95 %.
					10	Normal.	Clear.	Small clot.	40	All mononuclear.

TABLE 2.—FINDINGS IN ELEVEN CASES OF EPIDEMIC MYELO-ENCEPHALITIS³

Case No.	Age	Onset	Nervous Symptoms	Reflexes	c.c. Amt.	Pressure	Character	Spinal Fluid Clot Formation	Cells per c.mm.	Differential Cell Count	Result
1	3 yrs.	Gradual.	Irritable.	Absent k. j's ; very sensitive.	20	Slight.	Clear.	None.	180	Mononuclear 100 %.	Recovered.
2	9 mos.	Gradual.	Irritable.	Absent ; very sensitive.	35	Marked.	Opalescent.	Present ; fine clot.	580	Mononuclear 97 %.	Recovered.
3	5 yrs.	Gradual.	Irritable.	Absent ; very sensitive.	50	Marked.	Opalescent.	Small clot ; fibrin shreds.	510	Mononuclear 93 %.	Recovered.
4	2 yrs.	Sudden.	Irritable.	Absent ; sensitive.	30	Moderate.	Clear.	Spider-web clot.	130	Mononuclear 87 %.	Recovered.
5	5 yrs.	Sudden.	Irritable.	Very sensitive.	40	Marked.	Slightly opalescent.	Fine clot.	250	Mononuclear 89 %.	Recovered.
6	4 yrs.	Sudden ; convulsions.	Irritable ; convulsions.	Kernig present ; neck rigid.	30	Moderate.	Clear.	No clot, but fibrin shreds.	90	Mononuclear 100 %.	Recovered.
7	4 yrs.	Sudden.	Irritable.	Absent ; sensitive.	45	Marked.	Slightly opalescent.	Spider-web clot.	120	Mononuclear 95 %.	Recovered.
8	7 yrs.	Fairly rapid.	Irritable ; coarse tremors.	Absent ; sensitive.	50	Marked.	Opalescent.	Spider-web clot and fibrin shreds.	210	Mononuclear 97 %.	Recovered.
9	3 yrs.	Sudden.	Irritable.	Absent ; sensitive.	30	Slight.	Slightly turbid.	Moderate clot.	70	Mononuclear in excess	Recovered.
10	9 yrs.	Sudden.	Irritable ; sensitive.	Double Kernig ; neck sign.	40	Moderate.	Clear.	Fibrin shreds.	200	Mononuclear 75 %.	Died.
11	3 yrs.	Sudden.	Irritable.	Double Kernig ; sensitive.	35	Slight.	Opalescent.	Spider web.	55	Mononuclear 87 %.	Died.

3. Most of these spinal fluids were sent me for examination by the Massachusetts State Board of Health, to which I am indebted for the privilege of having had this opportunity of studying the spinal fluid from early human cases.

TABLE 3.—MENINGISM OR TOXIC-MENINGEAL IRRITATION DURING INFECTIOUS DISEASES

Case No.	Age	Onset	Mental Condition	Reflexes	Amount, c.c.	Pressure	Character	Clot Formation	Cell Count per cu. mm.	Differential
1	2 yrs.	Pneumonia.	Stupor.	Rigidity of neck ; Kernig sign.	First exam., 20	None.	Clear.	None.	5	All lymphocytes.
2	2¾ yrs.	Infectious diarrhea.	Dull ; delirious ; convulsions.	Neck sign ; Kernig sign.	Second exam., 15	Moderate. Slight.	Opalescent. Clear.	Spider web. Fibrin shreds.	40 45	All lymphocytes. All mononuclear.
3	5 mos.	Pertussis.	Delirious.	Kernig ; rigidity of neck.	6	None.	Clear.	Small clot.	10	All lymphocytes.
4	20 mos.	Otitis media.	Dull ; delirious.	Muscular tremors ; rigidity of neck.	10	Slight.	Clear.	Fibrin shreds.	90	All lymphocytes.
5	3 mos.	Otitis media.	Delirious ; convulsions.	Muscular twitchings ; Kernig ; neck sign.	First exam., 30 Third exam., 14	Marked. Slight.	Clear. Clear.	Fibrin shreds. Fibrin shreds.	80 20	Lymphocytes 90 %. All lymphocytes.
6	4 yrs.	Secondary anemia.	Dull ; semiconscious.	Placid ; all absent.	10	Slight.	Opalescent.	Small clot.	200	Polynuclears 61 %.
7	5 yrs.	Lobar pneumonia.	Convulsion.	Kernig ; neck sign ; rigidity of neck.	20	None.	Clear.	None.	50	Mononuclears 39 %.
8	6 yrs.	Lobar pneumonia.	Delirious ; convulsions.	Rigidity of neck ; Kernig.	80	Moderate.	Opalescent.	Fibrin shreds.	80	Lymphocytes in excess. Lymphocytes in excess.

lymphocytes, the occurrence also of fibrin, and a turbidity as marked as is found in any case of tuberculous meningitis.

Table 2 will show these findings and the different degrees of variation which each may undergo.

A third series of cases is reported (Table 3) which do not occur as often as the first two series, especially at the time of an epidemic. However, it is a condition that occurs frequently in acute infections, and which commonly gives a spinal fluid identical with that found in tuberculous meningitis, except for the absence of the tubercle bacillus.

It is plain from the study of these three tables that the spinal fluid reacts in the same way to a group of very different infections. Similar tables could be made from still more widely differing conditions as, for instance, syphilis. But as cerebral syphilis, or syphilis of the central nervous system, is rare in children, I have had the opportunity of examining only one such fluid, in which there was an increase in the mononuclear cells as well as an increase in the amount and pressure, but without any clot formation.

A study of 248 cases of tuberculous meningitis, with over 300 spinal fluid examinations shows the wide range of difference in the special observations and brings out the following points of interest:

The amount varied from 5 c.c. to 120 c.c., with occasionally dry taps. The fluid was usually clear to opalescent, but on several occasions turbid fluid was reported with very high cell-counts. Clot formation was absent in a little less than 10 per cent. of the examinations, but was usually present at some one of the examinations in every case. The clot also varied from the typical spider-web clot which forms in the course of several hours to one that forms almost immediately, and is of a pronounced gelatinous character. The cell count, which is made in one of the ordinary counting chambers, varied from fourteen to 920 cells per cu. mm., the average being 206 cells per cu. mm.; but 50 per cent. of the counts were 100, or below, so that such a high average is very misleading.

The differential count varied between 100 per cent. of lymphocytes and mononuclears and 89 per cent. of polynuclears, to 11 per cent. of mononuclears in one case. There were twenty-five instances in which the percentage of polynuclears was 30 per cent. or over. On repeated examinations this, however, would revert to the ordinary mononuclear count of over 90 per cent.

In a study of 102 cases from different forms of pyogenic meningitis, the epidemic meningococcus meningitis predominated; the findings also varied over a fairly wide range. The amounts varied from simply a slight amount of exudate in the needle to 250 c.c. of turbid fluid. In three cases only has clear fluid been found with the

TABLE 4. FINDINGS IN THE SPINAL FLUID IN THE VARIOUS TYPES OF MENINGITIS

Types	Amount of Spinal Fluid c.c.	Pressure	Character of Fluid	Presence of Fibrin	Cell Count per c.mm.	Differential Count	Organisms
Tuberculous meningitis.	10 to 100	Moderate.	Clear to opalescent.	On standing, fine clot.	15 to 200	Mononuclears predominating except in few acute cases.	Tubercle bacillus.
Epidemic cerebrospinal meningitis.	10 to 100	Marked.	Cloudy.	Marked.	100 to 800	Polynuclears predominating except in chronic stage.	<i>Diplococcus intracellularis</i>
Pneumococcus and streptococcus, Other meningitis.	+ to 100	Marked.	Cloudy.	Marked.	100 to 800	Polynuclears predominating.	Pneumococcus, streptococcus.
Encephalitis, Anterior poliomyelitis, Meningismus or toxic meningeal irritation.	10 to 80 10 to 50 Slightly plus.	Slight. Slight. Slight.	Opalescent, to cloudy. Clear. Clear.	Absent to slight. Present early; absent late. Usually absent; occasionally very small clot or shreds of fibrin.	40 to 400 10 to 100 10 to 100 10 to 80	Polynuclears predominating; in influenza at times mononuclears predominating. Mononuclears. Mononuclears during acute stage; polynuclears late if at all. Mononuclears.	Various organisms. None. None. None.
Normal.	5 to 10	None.	Clear.	Absent.	1 to 5 per cu. mm.	Mononuclears or endothelial cells.	None.

presence of the meningococcus. The clot formation was always present in abundance in all except these three cases, in which the clot was very fine, and resembled in every way that of the other types of meningeal irritation mentioned. The cell-count varied from forty-five cells per cu. mm. to 2,600, and in many cases the exudate was too thick to make even an approximate count. The differential count almost invariably gave a preponderance of polynuclear cells. In the chronic ones the mononuclear cells usually were equal to or in excess of the polynuclear cells; and during the treatment of meningococcus meningitis by its specific antiserum, the mononuclears would increase to the same extent as in the chronic cases.

Table 4 shows the wide range of findings in the spinal fluid from the cases discussed and shows very clearly the non-specific character of the cell-findings. It is evident from this study that the study of cell morphology alone in the spinal fluid of different meningeal conditions is not sufficient to separate the different types of meningitis, and therefore the diagnosis can never be based on this. The infecting or causative organism must be found in all cases in which there is a direct infection. A negative finding gives very little aid toward the positive diagnosis, though it has a value which increases with the clinical study of such cases. This makes the careful clinical study all the more important.

This short study has been confined to the cytology. The study of the spinal fluid from a chemical standpoint has not been attempted in this paper, nor has any mention been made of it in the tables. In the tables, however, a few of the more important symptoms and gross findings are tabulated, simply with a view toward showing that the clinical features of these cases also resembled each other very closely.

In conclusion, it is evident, first, that there are many conditions that give the same cytologic findings in the spinal fluid: (a) encephalitis, (b) epidemic myelo-encephalitis, (c) meningismus, (d) tuberculous meningitis, (e) syphilis of the central nervous system; second, that the presence of mononuclear cells or lymphocytes in the spinal fluid cannot be the basis for a diagnosis of tuberculous meningitis; third, that the recovery from animal inoculation, or the finding of the tubercle bacillus microscopically are the only positive means of making the diagnosis of tuberculous meningitis; fourth, that the study of the spinal fluid, although very important, must go hand-in-hand with more careful clinical studies of such border-lying cases as the ones shown in the different tables.

PROGRESS IN PEDIATRICS

ANATOMY, PHYSIOLOGY AND HYGIENE

Fresh Air Schools

(*J. Perkins. Boston Med. and Surg. Jour., clxiv, 10*)

Fresh air schools are for children physically below par, whether they have latent tuberculosis or not. Due to the active tuberculosis campaign, it has been shown that the majority of these children, and a certain percentage of children who appear in perfect health, have tuberculosis. Children with active tuberculosis should never be permitted in the public schools, but the others, with arrested, apparently cured or latent tuberculosis, can be benefited by the fresh air school. In Providence, R. I., fresh air schools have been conducted for three winters. The school rooms are open to the south. The air in the room is thus as pure as out-of-door air. Foot rugs and chairs with high backs are used to keep the children warm. Caps and mittens are worn. A hot drink is served at 10 o'clock and a lunch at 12. There is a single session, so the children reach home before dark. The homes of the children are visited and instruction in hygiene given. The children almost invariably gain weight, the hemoglobin in the blood rises and the general appearance is markedly improved.

RICHARD M. SMITH.

METABOLISM AND NUTRITION

Production of Glycosuria by Epinephrin in Thyroidectomized Dogs

(*F. P. Underhill. Am. Jour. Physiol., 1911, xxvii, 331*)

This work substantiates an earlier one by Underhill and Hilditch, which has been criticized by Falta and Rudinger. They performed another series of experiments on thyroidectomized dogs (the parathyroids were not disturbed) in which they confirmed their earlier findings, that subcutaneous doses of epinephrin (adrenalin chlorid) of 1 mg. per kilo of body weight caused glycosuria.

FRITZ B. TALBOT.

Experimental Contribution to the Study of Tetany in Childhood

(*V. Pexa. Arch. f. Kinderh., liv, Bk. 1-3, p. 1*)

Pexa investigated the cause of tetany and of the "spasmophilic diathesis." Former investigators had attributed the increased irritability of the peripheral nerves present in this disease to a diminution of the calcium present in the body and especially in the brain. Quest had found that an animal on a diet poor in calcium exhibited an increased irritability of the peripheral nerves. The object of Pexa's experiment was to investigate the truth of this finding. He therefore fed a dog for seventy-five days on a diet entirely free from calcium. Another dog of the same age and size was fed on an ordinary diet. From time to time electrical tests were made to determine the irritability of the peripheral nerves in both dogs. At the end of seventy-five days both dogs were killed. The dog on a calcium-free diet did not give any evidence of tetany. The irritability of the peripheral nerves was not increased; the general nervous condition of these dogs was one of marked apathy and stupidity. The brain of the dog which had been fed on a calcium-free diet showed a much smaller amount of calcium than did that of the control animal. Pexa considers that this experiment disproves the two theories proposed before. i. e. (1) that a diet free from calcium will cause an increased irri-

tability of the peripheral nerves and tetany; (2) that a lessened calcium content of the brain will lead to tetany. Pexa thinks that the cause of tetany is to be found elsewhere; that is, in an imperfect action of the parathyroid gland. He examined the parathyroid gland of the dog fed on a calcium-free diet and found no anatomic changes, but found the glycogen content much increased. He comes to the following conclusions: 1. The most striking feature of the clinical picture is a passivity of the animal toward external stimuli. 2. Absolute lack of an increased electrical irritability of the peripheral nervous system. 3. Marked diminution of the calcium content of the central nervous system. 4. Increased glycogen content of the otherwise unchanged parathyroid glands.

G. L. MEIGS.

Malnutrition in Infancy and Its Relation to Gastric Digestion

(L. J. Tint and L. Breskman. *Proc. Path. Soc., Phila., December, 1910, p. 260*)

Malnutrition as a cause of infant mortality occurs commonly in breast-fed as well as in artificially fed infants. Such children, without apparent cause, have green stools, vomiting and loss of weight, which gradually prove fatal. Slight changes in the quality and quantity of the feeding may disturb the delicate balance of the child's digestion and result in an attack of acute indigestion. The quantity of fat in the regular milk-supply may vary from day to day as much as from 4 to 12 per cent., and, in the experience of Tint and Breskman in the children's department of the Philadelphia General Hospital, this variation in the fat resulted in occasional outbreaks of vomiting. Careful preparation of the feedings and regulation of the amount of fat led to a cessation of vomiting. Some children, however, in whom the gastro-intestinal disturbance was well established, continued to vomit and pass green stools, with gradual loss of weight. Gastric lavage relieved the condition in some instances, but in others it failed. In order to ascertain whether free hydrochloric acid was absent in cases of malnutrition the authors analyzed the gastric contents of a number of such cases and compared them with like analyses of the gastric contents of children without gastro-intestinal disturbance. The results were as follows: 1. The examination of the gastric contents of eleven children, mostly under 1 year of age, without vomiting and green stools, showed the constant presence of free hydrochloric acid, rennin and pepsin. 2. Examination of the gastric contents of twenty children under 1 year of age, with green stools, vomiting and gradual loss of weight, showed an absence of free hydrochloric acid, rennin and pepsin. 3. In well-developed cases of malnutrition, such an absence of gastric activity was constant and persisted throughout the course of the affection. They deem the following points worthy of further study: 1. The stomach very early in life plays an important rôle in digestion through its peptic and rennin activities. Free hydrochloric acid is normally present. 2. With the onset of green stools in artificially fed and in breast-fed children, there is an absence of free hydrochloric acid. 3. The absence of gastric activity is relatively constant in children suffering from malnutrition. 4. Milks should be carefully examined for the fat percentage, when that is taken into consideration in making up feedings, particularly in asylums for children.

J. B. C.

The Relation of the Chemical Composition of Human Milk to Chronic Diarrhea and Eczema in Nurslings

(W. J. Maloney. *Practitioner, February, 1911*)

Maloney found that diet and exercise seem to have little or no influence on the sugar and fat content of human milk. Menstruation may coincide with marked impoverishment in fat. The amount of fat in milk varies as the hour and phase of the feed, and also according to individual peculiarities of mothers; a rigorous maternal régime does not appreciably influence the richness of the milk in fat; but an impoverishment may appear simultaneously with the menses.

The lactose of human milk is remarkable for the constancy of its amount, which seems indifferent to feeds, days, régimes and menstrual periods. In sixteen milks examined by Maloney, varying in age from 3 weeks to 7 months, the amount of lactose was only once below 5.28 per cent., and twice above 6.50 per cent. The average age of these milks was 3.12 months, and the average percentage of lactose they contained was 5.82. The percentage of lactose usually attributed to human milk seems, therefore, to be too high. Diarrhea in breast-fed infants whose feeding is carefully directed, may persist in some cases owing to excess of fat in the milk; in others, either owing to the presence of an abnormal laxative principle in milk, or to the undue irritability of an otherwise normal intestinal tract. In none of Maloney's cases could excess of sugar be incriminated. A state of chronic diarrhea prevailed in seven nurslings whose feeding was carefully directed, and whose food was not abnormally rich either in fat or in lactose. Regulation of the mother's régime did not influence this diarrhea. Three to six, usually four, motions occurred daily; they were characteristically of a light yellow color, semi-fluid, inoffensive and without curds. The infants steadily gained in weight, were apparently content, enjoyed an average amount of sleep, and were not unduly querulous. Four of these babies had a history of a persistent tendency to looseness of the bowels from birth. This benign diarrhea resulted, therefore, says Maloney, either from some relatively harmless laxative principle in the mother's milk, or from an excessive irritability peculiar to the infant's intestine. If, on transferring the child for a time to a healthy wet-nurse whose own charge was progressing normally, the diarrhea should cease, the mother's milk would be proved abnormal; if, however, it should continue, the infant's intestine would be proved hypersensitive. The three or four motions each day represented the child's habit. The only treatment required was to discourage weaning and to reassure the mother; for her benefit a little bismuth was usually given to the child. Eczema may arise in nurslings from overfeeding, from richness of the milk in sugar, and from the influence of a faulty maternal hygiene on the chemical composition of the milk. But undoubtedly it may, as in Maloney's six cases, exist in the absence of overfeeding, and when the milk contains only a normal amount of sugar. It may remain unaffected by the sacrifice of all the maternal indiscretions of diet. Probably it may arise independently of its commonly alleged factors; yet the coexistence of diarrhea and eczema in three babies makes Maloney reluctant to exonerate the milk-supply in any case of eczema occurring in a nursling.

F. C. ZAPFFE.

ACUTE INFECTIOUS DISEASES

Treatment of Acute Poliomyelitis

(W. E. Paul. *Boston Med. and Surg. Jour.*, 1911, *clxiv*, 46)

The care of poliomyelitis may be divided into three stages: acute illness, convalescence and the treatment of the permanently damaged structures. In the first stage rest is the one important measure. In the early convalescent period there is a tendency to contracture which must be prevented by splinting, etc. No active measures should be instituted so long as pain continues. The average period of rest is from four to six weeks. In the convalescent stage the chief means of treatment are electricity, active and passive exercises and massage. Electrical treatment must be intelligently given by a physician trained in the use of electrical apparatus. These measures may be kept up with benefit for a year or more.

With the cessation of improvement the condition of permanent crippling is to be considered. Operations and apparatus may do much to improve these deformities.

RICHARD M. SMITH.

Infantile Paralysis*(R. W. Lovett. Am. Jour. Pub. Hyg., 1910, xx, 875)*

Lovett has studied the epidemics of this disease in this country in relation to means of spreading, etc. It has been stated that the epidemic of 1907 in New York was due to infection brought over from Sweden. It was found on investigation that there was a decided increase in the total immigration just prior to 1907, but a sharp falling off in Scandinavian immigration. It has been repeatedly shown that the disease follows the lines of traffic. The steam and electric railroad travel has greatly increased during the last few years, as shown by statistics of the roads. The increase in automobiles may also be a factor in the situation. The disease occurs in summer, so the question of fruit, dust and insects were investigated. Fruit has not increased it, according to statistics. There has been excessive dryness in the last five years, but not especially in the affected regions. There are no satisfactory data in regard to insects. In general, the epidemic occurs in river valleys and not in coast towns. A small community, affected one year, is likely to be free the next, but this is less applicable to a large area. There is a suggestion of two-year periodicity in the occurrence of the epidemic. It is our duty to advise quarantine and the non-attendance at school of children from affected families.

RICHARD M. SMITH.

Spread of Scarlet Fever and Diphtheria in Schools*(C. V. Chapin. Amer. Jour. Pub. Hyg., 1910, xx, 813)*

The view is generally held that the intercourse of children in schools is a common cause of the spread of scarlet fever and diphtheria. The author studied the reported cases of these two diseases among school children in Providence for the years 1903-1908. This study showed that scarlet fever exhibited a marked decrease before the summer vacation each year, and that diphtheria decreased in three out of the five years. In half the instances the autumnal increase in the diseases began before the school opened. He concludes that the decrease in these two diseases is associated with temperature changes. A similar study of all cases of scarlet fever and diphtheria for the ten years ending 1903, shows the same lack of connection between the prevalence of the disease and school attendance. Since the incubation period of these diseases is short, if school attendance had any influence on their prevalence, it might be shown even in the short vacations. In Providence there was a decrease of the diseases twenty-one times in the week following the short vacation, an increase twenty-times and the number remained the same eight times. Another reason for doubting that school attendance greatly influences the prevalence of these diseases is that they are more common in children under school age than among those of school age. A tabulation of the cases for twenty years shows an increase for each year of life up to 6, after which there is a yearly decrease. It is quite possible that a certain amount of infection does take place at school, and this should be guarded against by every precaution. Disinfection of the school is useless. The trouble comes from "missed cases" or fever carriers. To prevent harm from them it is necessary to reduce to a minimum the chances of exchange of saliva or other secretions.

RICHARD M. SMITH.

Acute Poliomyelo-encephalitis*(J. L. Morse. Boston Med. and Surg. Jour., 1911, clxiv, 41)*

Acute poliomyelo-encephalitis is due to an ultra-microscopic organism. The virus is filterable, withstands glycerinization and drying over caustic potash, is not impaired by freezing, but is injured by heating and is destroyed by 1 per cent. H_2O_2 and by menthol. It is doubtful if it has been cultivated outside the body. Inoculation experiments in all warm-blooded animals, except monkeys, have been unsuccessful. Infection has been produced by injections intracerebrally, intraperitoneally, intravenously, into the spinal canal, into large nerves and through

certain mucous membranes, especially of the nasopharynx. The virus escapes through the nasopharyngeal mucous membrane. The disease is contagious, but not highly so. It is probable that the virus gains entrance to the body through the nasopharynx, and it is possible that there may be "carriers" who spread the disease. The period of incubation varies experimentally from three to thirty-three days, the average being eight to nine days. Clinically it may be as short as twenty-four hours. Patients with the disease should be quarantined. Morse has adopted three weeks as the length of time for the quarantine, but it would be of advantage for the State Board of Health to set some arbitrary limit. To prevent the spreading of infection hexamethylenamin should be given to patients during the acute stage of the disease and to persons exposed. The nose of those ill and those exposed should be sprayed with hydrogen peroxid. A second attack is rare, but at present it is not justifiable to attempt to induce active immunity as a protective measure. In general, children should not be taken to places where infantile paralysis exists, or if there, should be kept away from other people. Wherever the virus enters it has a predilection for the nervous system. The vascular lesions constitute the primary cause of the lesions of the nervous tissue. Cellular infiltration changes are set up which are most marked in the perivascular lymph-spaces of the arteries entering the nervous tissue. All parts of the central nervous system may be involved. Our conception of the disease must be enlarged to include acute poliomyelitis and myelitis. A better term for the disease than poliomyelitis or infantile paralysis would be poliomyelo-encephalitis. Wickman's classification is the best, giving eight forms—the ordinary spinal paralysis; progressive paralysis, usually ascending, including Landry's paralysis; bulbar paralysis; encephalitis, giving spastic, monoplegia or hemiplegia; ataxic form; polyneuritic type; meningitic form and the abortive form. The diagnosis at present is impossible before the appearance of the paralysis. The triad of symptoms—sweating, irritability, and hyperesthesia—are not constant. The leukocyte count is so variable as to be of little value. The diagnosis could be made early by examination of the spinal fluid, but it would be necessary to do lumbar puncture on every sick child in the summer, and this is not a rational procedure. Prognosis as to life and recovery from paralysis cannot be made early in the disease. The treatment during the early stages of the disease consists in giving hexamethylenamin, rest and preventing contractures.

RICHARD M. SMITH.

Observations and Results of Investigation in the Epidemic of Poliomyelitis in Steiermark in 1909

(Karl Potpeschnigg. *Arch. f. Kinderh., liv, Bk. 4-6, p. 343*)

In August, 1909, the author sent letters to 470 physicians in the province of Steiermark in regard to the epidemic of poliomyelitis which had been raging there during that year. About one-half the physicians answered, reporting about 600 cases; in his own clinic he observed sixty-six cases. He makes them the basis for the following observations:

In regard to contagiousness he observes: 1. In favor of contagiousness are these facts: Very often there are many cases in one family. Neighbors and persons coming in contact with those having the disease are often attacked. Large numbers of cases occur in one neighborhood.

2. Against contagiousness are these facts: There are no cases of epidemics in hospitals. The disease does not develop in many cases in which the contact is very close and long. In many instances there are only isolated cases, although there is no quarantine. He concludes, therefore, that contact infection is very probable, but can only be made certain by the discovery of the cause.

The incubation period he estimates at six to ten days in most cases. The onset and prodromal period were variable in their manifestations. The prodromes were sometimes lacking; the child went to bed well one night and was found paralyzed the next morning. Fever was usually present, ranging sometimes from 102 to 105 F. Sometimes it was normal or low. Tonsillitis in one-

third of his cases was described as occurring before the paralysis. Throat cultures were made in many of the cases; usually a mixed flora was present. In one case a pure culture of the *Staphylococcus albus* was obtained. Gastro-intestinal disturbances were rarer in this epidemic than tonsillitis; the author, however, observed several cases of severe gastro-enteritis. In the cases coming to autopsy Peyer's patches were found swollen. Vomiting was often present.

Leukopenia.—The author saw so few cases in their initial stage that he could not investigate the point of an early leukopenia. In the stage of paralysis the leukocytes were 8,000 to 12,000. The differential blood count showed nothing abnormal.

Initial Nervous Symptoms.—Headache was very often present, localized in the back of the head and very severe. Stiffness of the neck and opisthotonos, with tenderness of the neck muscles were found to be early diagnostic symptoms.

Pain.—Pain was often marked in the peripheral nerves, muscles and joints. Darting pains through the chest and under the shoulder blade were observed several times.

The author concludes that the initial symptoms are so variable as to make an early diagnosis very difficult.

The Stage of Paralysis.—Distinct paralysis was often preceded by a reduction of motor power. Muscular fatigue during this stage seemed to increase the paralysis greatly. Increase and course of the paralysis was often remarkably rapid. He cites a case in which only nine hours elapsed from the beginning of paresis till the death of the patient from paralysis of respiration. These cases early in the epidemic were diagnosed as Landry's paralysis. The spread of the paralysis in other cases was much slower. The paralysis often continued to extend for several days after the temperature had fallen. Paralysis of the bladder often occurred early, but was never permanent. Among his own cases were six cases of vesical paralysis, all connected with paralysis of the lower extremities. Obstipation was noted sixteen times. Pain was marked also during the paralytic stage and led to cramped positions of the limbs and to the development of contractures. Disturbances of sensory, trophic, vasomotor and heat-regulating nerves were often present. There was often increased perspiration, and in several cases desquamation of the skin resembling that after scarlet fever. Facial paralysis was noted six times; most often associated with the cerebral form of the disease, resembling meningitis.

Paralysis of the muscles of deglutition was present only in the rapidly fatal forms. Increase of the deep reflexes was quite often noted. The permanent paralysis affected most often certain groups, as the peronei, deltoid or quadriceps. The lower limbs were much oftener affected than the upper.

Abortive cases were not observed at the clinic, but many were reported from the epidemic. The mortality in this epidemic was 13.1 per cent. For children under school age it was lower—7.5 per cent.; for adults, higher—24.24 per cent. All deaths were from paralysis of respiration. Quite frequently death occurred on the fourth day of the disease.

Lumbar puncture was made forty-eight times on thirty-five children. In all cases a perfectly clear fluid was obtained. On standing, a filmy coagulate, resembling spider's web, was formed. In the majority of cases the protein was increased, the sugar diminished. The pressure of the fluid was often increased and was often so high that the fluid spurted out. The pressure was not measured.

Bacteriologic examinations were made in all cases; in twelve cases Gram-positive diplococci were grown. In two cases the same organism was obtained in smears made from the spinal gray matter. In all other cases the cultures were sterile.

Animal experiments were carried out. Apes, rabbits and guinea-pigs were injected intravenously, intraperitoneally and into the spinal canal with spinal

fluid from cases in the acute and paralytic stages. In no case did paralysis result. Blood cultures were made from several patients. In two cases an organism was obtained similar to that from the spinal puncture. G. L. MEIGS.

GASTRO-INTESTINAL SYSTEM

Proctoscopy and Sigmoidoscopy in Infancy

(H. L. Bowditch. *Arch. Pediat.*, January, 1911)

In twenty-four cases of infectious diarrhea, Bowditch examined the rectum and sigmoid by inspection. He found that cases of diarrhea in which there is a history of blood in the stools (especially among infants), show signs of inflammation (red, thickened mucous membrane, prominence of the follicles, ulcers of varying types, but no true membranous condition) throughout the sigmoid and rectum, especially during the acute stage of the disease. These lesions seem to vary, according to the virulence of the infection, as to number and general appearance. They gradually become healed, leaving no signs nor evidence of scar tissue visible to local sigmoidal inspection in life. Bowditch also found that blood and normal intestinal mucous membrane may be present, at least in the sigmoid and rectum, in cases of fermentation diarrhea. Of the severer types of cases all but two patients received one or more irrigations, three had four and two received none. No sign of any healthy appearance was found in these cases, neither did the mucous membrane of those treated, or those untreated, differ in any appreciable way. Of those cases of milder type, all but two patients received silver nitrate irrigations. Three got a single irrigation early in the disease, five had more than two, and at the most, three irrigations. While a gradual improvement was apparent at the end of these repeated irrigations, at no time did the mucous membrane after a single treatment show any distinct betterment.

F. C. ZAPFFE.

RESPIRATORY SYSTEM

The Diagnosis of Pleuritic Effusions in Infancy

(D. J. M. Miller. *Arch. Pediat.*, January, 1911)

Miller emphasizes the following points: Pleurisy with effusion is a common affection in infants under 2 years of age. In the vast majority of cases it is purulent. Because of the disastrous, and even fatal, results of delay in or mistakes of diagnosis, it should be recognized early, so that prompt—that is, surgical—treatment may be instituted. The diagnosis is often obscure, demanding, in the highest degree, carefulness, skill and experience. In arriving at a diagnosis, the antecedent affections should be fully appreciated. Of these, pneumonia is by far the most common. The general symptoms, as well as the physical signs, should be carefully weighed and considered. Of these, the latter are the more distinctive. The most reliable signs, in the order of their importance, are (1) exploratory puncture, (2) dullness with a sense of resistance, and (3) displacement of the apex. The other physical signs, so valuable in differentiating effusions in the adult, are uncertain, variable and confusing, and cannot be relied on in infants. The recognition of localized collections of fluid is especially puzzling, and demands great skill and watchfulness and a frequent resort to exploratory puncture or operation. The latter is safe, even when the lung is pierced, and particularly so when fluid is present. Notwithstanding the rare accidents that have followed this procedure, it should be employed to determine the character of the fluid, and, owing to the distressing results of unrecognized empyemas, it is imperatively demanded in all doubtful cases. The variability of the physical signs is a striking feature in infants and should always suggest an effusion.

F. C. ZAPFFE.

BLOOD AND CIRCULATORY SYSTEM

Acute Lymphatic Leukemia in an Infant

(B. S. Veeder. *Arch. Pediat.*, January, 1911)

The count in his case, which reached 1,330,000, is the highest leukocyte count which Veeder has been able to find on record in lymphatic leukemia in childhood. E. H., female, aged 17 months, was brought to the hospital for a purpuric eruption, which was said to have appeared five days before admission. Practically no history could be obtained. The child had been breast-fed. A swelling of the neck had appeared "some time" before the eruption. The skin was pale and showed a widespread purpuric eruption, varying in size from small, bright red petechial spots about pinhead in size, to large subcutaneous extravasations, cyanotic in color, and about the size of a 25-cent piece. The large extravasations were present over the forehead, extensor surface of the forearms, the tibiae, and over the spines of the lumbar vertebrae; the smaller lesions were most marked over the face, right shoulder and legs. Pressure over the bones did not produce pain nor signs of tenderness. The joints were uninvolved. The mucous membranes of the mouth were pale, but showed numerous points of hemorrhage. The saliva was slightly blood-streaked. The tonsils were large, swollen and red, almost shutting off the mouth cavity from the pharynx. The cervical lymph-nodes were enlarged and palpable. They were moderately soft in consistency and about the size of a hickory nut. Pressure over the right side of the neck seemed to cause pain. The axillary and inguinal nodes were both enlarged and distinctly palpable as separate tumors about the size of lima beans. The interesting feature of the case is the blood examination: Hemoglobin, 55 per cent.; erythrocytes, 3,370,000; leukocytes, 1,330,000. The field under the microscope was densely packed with lymphocytes, these being so numerous as to obscure practically everything else. The lymphocytes showed two distinct types, a small and a large cell variety, but between these two extremes there were so many gradations in size that an accurate subdivision of many of the cells into large or small lymphocytes was impossible. The differential count (1,000 cells) was as follows: Lymphocytes, 98.5 per cent.; polymorphonuclears, 1.2 per cent.; myelocytes, .3 per cent. One nucleated red was found during this count.

F. C. ZAPFFE.

NERVOUS SYSTEM

Data and Tests in the Study of the Exceptional Child

(M. P. E. Groszmann. *Brit. Jour. Dis. of Children*, vii, 481)

Apparent disinclination to mind may be due to imperfect hearing; aversion to reading and writing to imperfect vision. Ugliness and irritability may be caused by astigmatism, which, in its turn, produces eye-strain and persistent headaches. Laziness may be a symptom of anemia or neurasthenia, or may be caused by malnutrition or over-exertion at home, lack of sleep or ventilation in the child's sleeping chamber. Fretfulness is often caused by indigestion. Giggling, babbling, whispering, sniffing, restlessness and inattention are often symptoms of some nervous disease. They may be enumerated among the various habit-tics or habit-spasms. Again, momentary inattention and absent-mindedness may be due to a mild form of *petit mal*. Sudden attacks of excitement, outbreaks of temper, destructiveness and hitting of other children, are indications of psychic epilepsy. While true hysteria is not recognized in children, still, emotional temperaments are often seen. Stubbornness and disobedience are danger signs and require further investigation. Realizing that body and mind are two aspects of the same personality, we must first endeavor to establish whether there has been normal growth in either direction. Just as the anatomic structure of a child may be either in advance or behind its years, likewise its mental, moral and volitional development may be accelerated or retarded. Any discrepancy between the stand-

ards of such development for any age is a danger signal. Proper and regularly repeated body measurements are most essential. Recently Professor Rotch has suggested an interesting test by taking *x*-ray pictures of the wrists and hands. The development of the carpal bones and lower epiphysis of radius and ulna are said to be indications of the structural age of a child. Close observations of the various physiologic functions of the body, grip of hand and weakness of any of the special senses, are of great value. Body symptoms will indicate psychic defects; psychic defects will indicate disturbance of physiologic function. The various tests devised by Dr. Sante de Sanctis, Dr. Binet and Groszmann are ingenious methods of measuring motor, sensory and intellectual capacities. The causes of some of the symptoms may be found not so much in the child, but in the home or in the relation of teacher to pupil, or the school curriculum may not be properly graded. The hygiene of the school room, and of the child's life outside of school, require attention. Children who sleep in unhygienic quarters, those who are made slaves outside of the school room and do not get proper rest, cannot possibly have a normal alertness. Children whose progress and conduct is irregular should be transferred to observation groups. Here, under a specially trained nurse and the pediatric expert, the case may be closely watched and inquiry into its family history and surroundings made. The child may be removed to a hospital, sanatorium or special school as the condition requires.

HERBERT J. BALDWIN.

GENITO-URINARY SYSTEM

Albuminuria in Infants

(*Francis Marre. Rev. d'Hyg. et de Méd. Inf., 1910, No. 2, p. 11*)

From a study of the urine of eleven infants less than a month old, Marre concludes that albuminuria in infants, even new-born, indicates a pathologic condition. Children of mothers with eclampsia or albuminuria of pregnancy may show albumin in the urine at birth; or later, secondary to a slight disturbance which would not produce albuminuria in a normal infant. This is believed to be due to a pathologic condition of the kidneys produced by absorption *in utero* of nephrotoxic substances from the mother's blood. With this exception, secondary albuminuria in infants is analogous to the same conditions in adults.

J. HERBERT YOUNG.

OSSEOUS SYSTEM

Enlargement of the Tubercle of the Tibia

(*R. C. Elmslie. Brit. Jour. Child. Dis., viii, No. 85, p. 9*)

Osgood and Schlatter described this condition as due to tearing off of the epiphysis of the tubercle, or a portion of it, by muscular violence. The accounts of the mode of ossification of the tubercle of the tibia vary considerably. Which-ever view is correct, it is certain that at the age of 14 the tubercle consists of a tongue-like process extending downward from the anterior part of the upper epiphysis of the tibia and separated from the shaft by a layer of cartilage. This process unites to the shaft from 18 to 24. Complete separation of the tubercle by violence is rare. Enlargement of the tubercle of the tibia in children of 12 to 18 was described by Osgood and Schlatter, as the result of partial separation of the tubercle by muscular violence in jumping and running. It is more common in boys than in girls, and usually comes at 14 to 16. The subjects are often athletes, and the trouble may come on some weeks or months after injury. The complaint is swelling of the tubercle, which is tender on pressure or painful when any exercise is taken in which the quadriceps is exerted powerfully. The pain may even persist at night. The skiagraphic pictures are typical. The pain-

ful condition may last for a few months, or for two years. In many cases the pain recurs at intervals, as a result of exertion of the quadriceps or of slight injury to the tubercle. Eventually the pain subsides, but a permanent enlargement of the tubercle persists. Enlargement of the tubercle may be mistaken for tuberculous disease of the head of the tibia or syphilitic periostitis. Treatment is symptomatic, rest, local anodynes or counterirritants during painful stages. As a rule, the pain subsides in a few months, and the knee may be used as freely as ever, although the swelling persists.

HERBERT J. BALDWIN.

THERAPEUTICS

Susceptibility of Animals of Various Ages to Opium Alkaloids

(*E. Döbeli. Monatschr. f. Kinderh., 1910, ix, 397*)

Döbeli used suckling and adult rabbits to determine the relative toxicity of opium in infancy as compared with adults. He concludes from his search through literature and his own experience that opium is not well borne by babies, but that older children probably can take as large doses per kilo of body weight as adults. Suckling rabbits are twice as sensitive to laudanum and morphin as the adult animal. There is no difference in the action of codein on the suckling or the adult.

FRITZ B. TALBOT.

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INFLUENZAL MENINGITIS, WITH ESPECIAL REFERENCE TO ITS PATHOLOGY AND BACTERIOLOGY *

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CHICAGO

Influenzal meningitis, on account of its rarity, has attracted little attention in medicine. However, as the condition is becoming better known, and especially since improved diagnostic methods have come into more general use, the number of cases reported from various countries is increasing each year and evidently they will soon cease to be uncommon. There has been a wide difference of opinion in regard to the significance of *B. influenzae* in infections, especially in ordinary influenza or "grippe." This is chiefly due to the fact that epidemics occur which in their clinical features are practically identical, but which appear to be caused by a variety of organisms in the respiratory tract. Whatever may be the outcome of this controversy, the occurrence of influenza bacilli in pure culture in cases of meningitis demonstrates conclusively that this organism may be highly pathogenic and therefore its presence in throats, sputa, etc., should not be regarded with indifference.

Recently the literature on the subject of influenzal meningitis has been analyzed by several writers. Adams,¹ Cohoe,² Cohen,³ and Wollstein⁴ have collected the cases and discussed their more important features. It is difficult to state just how many cases should be included as primary influenzal meningitis, because mixed infections occurred in a considerable number. It is undoubtedly true, however, that in many if not in all of the cases of mixed infection the influenza bacillus was the primary invader of the cranial cavity, for the reason that cocci which were found associated with influenza bacilli are very common secondary invaders, whereas influenza bacilli are rarely found as such. The cases are widely distributed, occurring in various countries in Europe and America. In general they may be said to be sporadic, there being no tendency for them to occur in epidemics; nor is there any clear associ-

*From the Pathological Laboratories of Rush Medical College.

1. Adams: Arch. Pediat., 1907, xxiv, 721.

2. Cohoe: Am. Jour. Med. Sci., 1909, cxxxvii, 74.

3. Cohen: Ann. de l'Inst. Pasteur, 1909, xxiii, 273.

4. Wollstein, M.: Am. Jour. Dis. Child., 1911, i, 42.

ation between their occurrence and epidemics of influenza or grip. It is a disease confined very largely to children under 1 year of age. Five cases have occurred in individuals over 20. The mortality is about 90 per cent.

The reports of Ghon,⁵ Fraenkel,⁶ Dubois,⁷ Cohoe,⁸ Cohen⁸ and Wollstein¹ give the most complete bacteriologic and histologic studies that have been made. More than half of the cases have come to autopsy.

Recently⁹ I reported the occurrence of this disease in twin brothers, with autopsy and bacteriologic findings in one. Since that time five other cases have been met with in Chicago, making seven in all, five of which have been examined post mortem. These cases are here recorded, special attention being given to the pathologic anatomy and bacteriology of the disease.⁹

CASES 1 AND 2.—Twin brothers were born by a healthy mother at full term in a normal condition. Five days later both infants became ill with symptoms of acute enteritis, associated later with muscular twitchings, cyanosis, stupor, and temperature ranging from 100 to 104 F. One child died on the fourth day of the disease and the other died on the seventh day, both having run almost identical clinical courses without definite meningeal symptoms. Autopsy was permitted in the first case only and was made by Dr. LeCount.

Anatomic Diagnosis.—Acute purulent leptomeningitis; acute parenchymatous degeneration of the heart, liver and kidneys; acute swelling of the spleen; multiple ecchymoses of the pleura and thymus; acute catarrhal gastro-enteritis.

B. influenza was found pure in smears and cultures of the meningeal exudate, cerebrospinal fluid and peritoneal fluid. In the heart's blood were a few *B. coli* but no influenza bacilli. In the cerebrospinal fluid were numerous cells, 80 per cent. of which were polynuclear leukocytes and both within and without these cells were enormous numbers of influenza bacilli.

Over the entire convex surface of the brain were well defined areas of greenish-yellow purulent exudate, irregular in shape and from 1 to several sq. cm. in size and 1 to 5 mm. thick. At the base, especially in the region of the optic chiasm and the pons, and along the larger blood-vessels, the deposit was more abundant and diffuse. No pathologic change was present in the nasal or tympanic cavities.

Microscopically the exudate was made up largely of polynuclear cells, there being also in places mononuclear and phagocytic endothelial cells in considerable numbers, but very little fibrin.

CASE 3.—Infant girl aged 13 months, admitted to nursery of Chicago Maternity, Sept. 22, 1908. The child did rather poorly at first, but later gained. On December 1 she contracted a cold, which was prevalent in the nursery. The temperature remained normal and appetite good until December 6, when the child showed signs of serious illness, the temperature rising to 101.6 F. The chest-findings suggested bronchopneumonia. The following day the symptoms became worse, the temperature rose to 103 F., and the child was isolated and treated for pneumonia. She was restless, coughed some and cried a good deal. The stools

5. Ghon: Wien. klin. Wchnschr., 1902, xv, 667.

6. Fraenkel: Ztschr. f. Hyg., 1898, xxvii, 315.

7. Dubois: Thèse de Paris, 1902, No. 49.

8. Davis, D. J.: Arch. Int. Med., 1909, iv, 323.

9. A short summary of these cases is given in Tr. Chicago Path. Soc., 1910, viii, 39, the pathological specimens having been shown to the Chicago Pathological Society in joint meeting with the Chicago Neurological Society, March 14, 1910.

remained normal and she took her food fairly well the first six or seven days of the illness. The child showed from the first a disinclination to have her head moved, and resisted handling. No retraction of the head was noticed until after the ninth day of her sickness, though she showed from the beginning slight rigidity of the neck muscles. On the seventh day the fever remained below 101 F., going down to 99.4 F., and the chest sounds indicated some abatement of the trouble, but on the ninth day the temperature rose again and ranged between 105 and 101 F. for the next five days, staying at 103 or thereabouts most of the time. The ears, nose and throat examined at this time were normal. December 12, the twelfth day of illness, the child seemed much worse. From this date rigidity increased, both sides being involved; there was some retraction of the head; contraction of the pupils, though not marked; a slight bulging of the fontanel and irregular breathing. The feet were edematous from contraction, and the bowel movements gave an offensive odor. The kidneys were acting normally. Mild convulsive attacks came on, lasting from twenty to thirty minutes. December 14 lumbar puncture was made. The fluid obtained was turbid, under pressure, and contained many polynuclear and few mononuclear cells. There were also small Gram-negative bacilli, both intra- and extracellular, which did not grow on plain media. The child failed rapidly and died that night.

Autopsy Report.—The autopsy was held one hour after death, and following is the anatomic diagnosis: acute purulent leptomeningitis (influenzal); acute bronchitis; bronchopneumonia; acute splenitis; cloudy swelling of the liver, heart and kidneys; acute swelling of the peribronchial lymph-glands; enlargement of tonsils; fatty liver; divergent strabismus.

The body was not emaciated. The pupils were equal and moderately dilated and the left eye diverged; no icterus. The anterior fontanel bulged slightly. In the peritoneal cavity were a few drops of clear fluid; in the pericardial cavity were a few cubic centimeters of slightly turbid fluid. The tonsils were dark red, slightly enlarged and the surfaces irregular. The nasal mucosa was reddened and in the upper part of the nasal cavity was a small amount of slightly purulent secretion.

The upper lobe of the left lung was normal. The lower lobe, especially in its posterior portion, was dark red and in places did not crepitate. On section regions were seen which were deep red in color and contained numerous small gray areas about 1 or more mm. across, from the centers of which exuded on pressure a small amount of pus. The tissue from these regions sank in water. No fibrin appeared on gross examination. From the larger bronchial tubes pus could be expressed.

The right lung in general resembled the left. The apex contained a small, slightly depressed region where crepitus was feeble and on section pus exuded from the smaller bronchi, which were surrounded by a narrow, light gray zone. The lower lobe was similar to the lower lobe of the left lung. The pericardium, heart, stomach, intestines, pancreas, adrenals and genito-urinary organs showed no noteworthy changes. The liver was fatty and the kidneys on section were dull red, soft, slightly swollen and the markings indistinct.

Brain and Spinal Cord.—There was an excess of distinctly turbid cerebrospinal fluid which appeared to be under increased pressure. Over the entire surface of the frontal lobes and in large patches over the other portions of the brain, especially the base, there was a thick, greenish-yellow, purulent exudate involving the pia-arachnoid. As a rule the exudate was more extensive in the regions of the blood-vessels and about the cranial nerves at the base. The vessels were intensely congested and the convolutions, especially over the frontal lobes, were very much flattened. No hemorrhages appeared. The dura was everywhere reddened, and at the base in places thick greenish pus adhered to its surface. The tympanic cavities showed no change.

The meninges of the spinal cord were intensely congested and a fibrino-purulent exudate was present throughout the canal.

Microscopic Examination.—Sections made of the cortex and meninges in the region of the larger vessels in the Sylvian fissure showed an extensive exudate in the pia. This consisted chiefly of polynuclear leukocytes, but in places mononuclear cells were common. Many of the former were disintegrated. The mononuclear cells had round or oval nuclei and a moderate amount of protoplasm. Plasma cells were rare. About the blood-vessels the exudate was abundant. Occasionally a few polynuclear and mononuclear cells were seen in the cortex near the surface and along the small blood-vessels penetrating the brain; no hemorrhages were found in the meninges or brain tissue. A similar exudate occurred in the cerebellum. The polynuclears were also abundant here and in places large phagocytic endothelial cells were common. In sections of the spinal cord were seen an extensive exudate in the meninges, especially enveloping the roots of the spinal nerves. Polynuclear leukocytes predominated but many mononuclear cells also occurred. There was intense congestion of the blood-vessels but no hemorrhages. Perivascular infiltration was beautifully seen about the small blood-vessels entering the cord from the pia. The central canal appeared unchanged.

In sections of the lung many polynuclear leukocytes were seen in the lumen of the bronchioles and the walls were intensely congested and infiltrated with round-cells and leukocytes. The alveoli in the region about the bronchioles usually contained exudate consisting of plasma-cells, leukocytes and, sometimes, fibrin. The tissue everywhere showed marked congestion and some edema. In the kidneys leukocytic casts were occasionally found in the tubules and in general the tubular epithelial cells were swollen and the nuclei stained indistinctly. A large amount of fat was seen everywhere in the liver. In the centers of the Malpighian bodies in the spleen areas of necrosis were often found. The myocardium, adrenals and thymus showed no significant changes.

Bacteriologic Report.—The cerebrospinal fluid was distinctly turbid but not bloody. In cover-glass smears were many polynuclear leukocytes and a few large mononuclear cells, and both within and without the leukocytes large numbers of very small bipolar Gram-negative bacilli were seen. Smears of the thick exudate showed the same bacilli and numerous leukocytes. Cultures of the fluid gave an abundant growth of typical *B. influenza*. On some plates were one or two colonies of *B. coli*, evidently a contamination, and about these the larger influenza colonies were grouped, showing characteristically their symbiotic property. Cultures of the heart's-blood gave on plates a pure growth of *B. influenza*. On some plates, purposely contaminated, numerous larger influenza colonies were grouped around the contaminating colonies. In smears and cultures made from the lung exudate *B. influenza* was found as the predominating organism. A moderate number of pneumococci were also present. In the pericardial fluid a few influenza bacilli were found in pure cultures. Examination of the peritoneal fluid and emulsions of the spleen and peribronchial lymph-glands for influenza bacilli gave negative results. A few colon bacilli were recovered from the peritoneal fluid. Careful search was made for influenza bacilli in the nasal secretion, but none was found. Many pus-cells occurred, and also a few staphylococci and many saprophytic organisms.

Serum from the heart's-blood obtained at the autopsy did not specifically agglutinate the bacilli from the spinal fluid, even in low dilutions. Animals were not highly susceptible. One c.c. of the cerebrospinal fluid injected immediately after the autopsy intraperitoneally into a guinea-pig was not fatal. The growth from two or three slants of pigeon-blood-agar given intraperitoneally was required to kill.

CASE 4.—Infant girl, colored, aged 7 months, admitted to the Maternity Hospital Nursery, May 27, 1909. The child contracted a cold in the early part of December, 1909, which persisted, but was not severe. January 1, the temperature was 102 F. January 2, the temperature was recorded as normal, but January 3, it was 100 F. at 9 a. m. and the child looked ill. At 11 a. m. the temperature rose to 103 F. and a little later a convulsion occurred which lasted

for some time. Rigidity persisted, and, meningitis being suspected, the child was taken to the Presbyterian Hospital, where she rapidly grew worse, suffering several convulsions, and died during the night. Spinal puncture was made a few hours before death and a turbid fluid under pressure was obtained. It contained many polymuclear and few mononuclear cells; also many small Gram-negative bacilli, both intra- and extracellular, which did not grow on plain media.

Autopsy.—The autopsy was made six hours after death and the following anatomic diagnosis given: acute fibrino-purulent leptomenigitis; catarrhal bron-

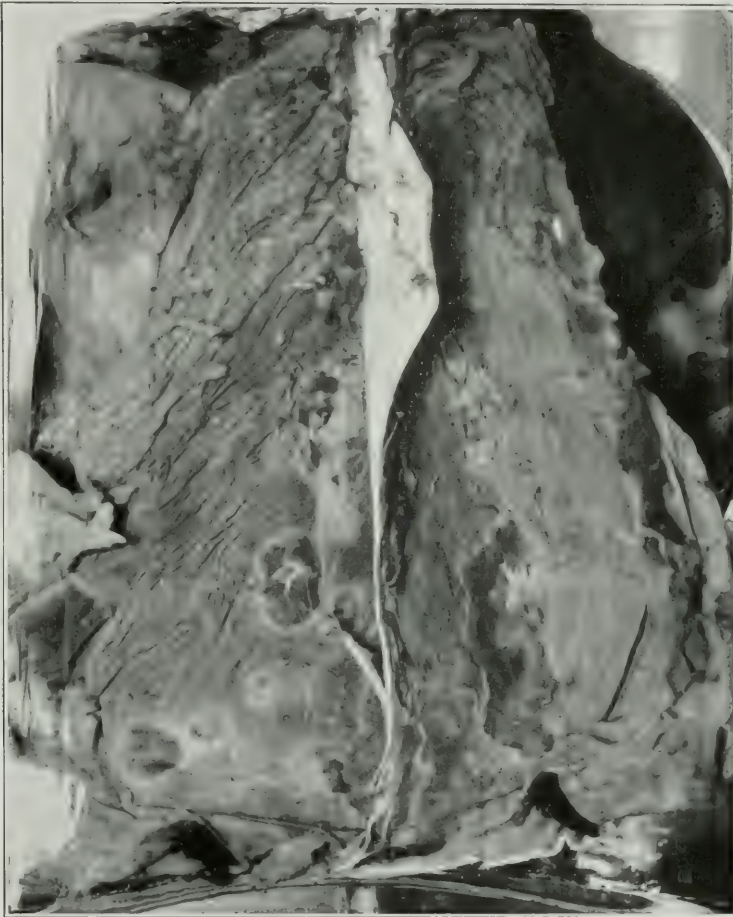


Fig. 1.—Photograph of the hemorrhagic pseudomembranous exudate lining the dura in Case 5. In places it has been detached from the dura.

chitis; acute rhinitis; edema and congestion of the lungs; acute splenitis; fatty liver; cloudy swelling of the heart and kidneys.

The child was well nourished. Both eyes deviated strongly to the left; the pupils were equal but dilated; no discharge from the ears. The peritoneal cavity contained a few drops, and the pericardial cavity a few cubic centimeters, of clear fluid. The thymus, thyroid, heart, larynx and pharynx presented no significant changes. The nasal mucosa was covered by a thin layer of tenacious mucus and

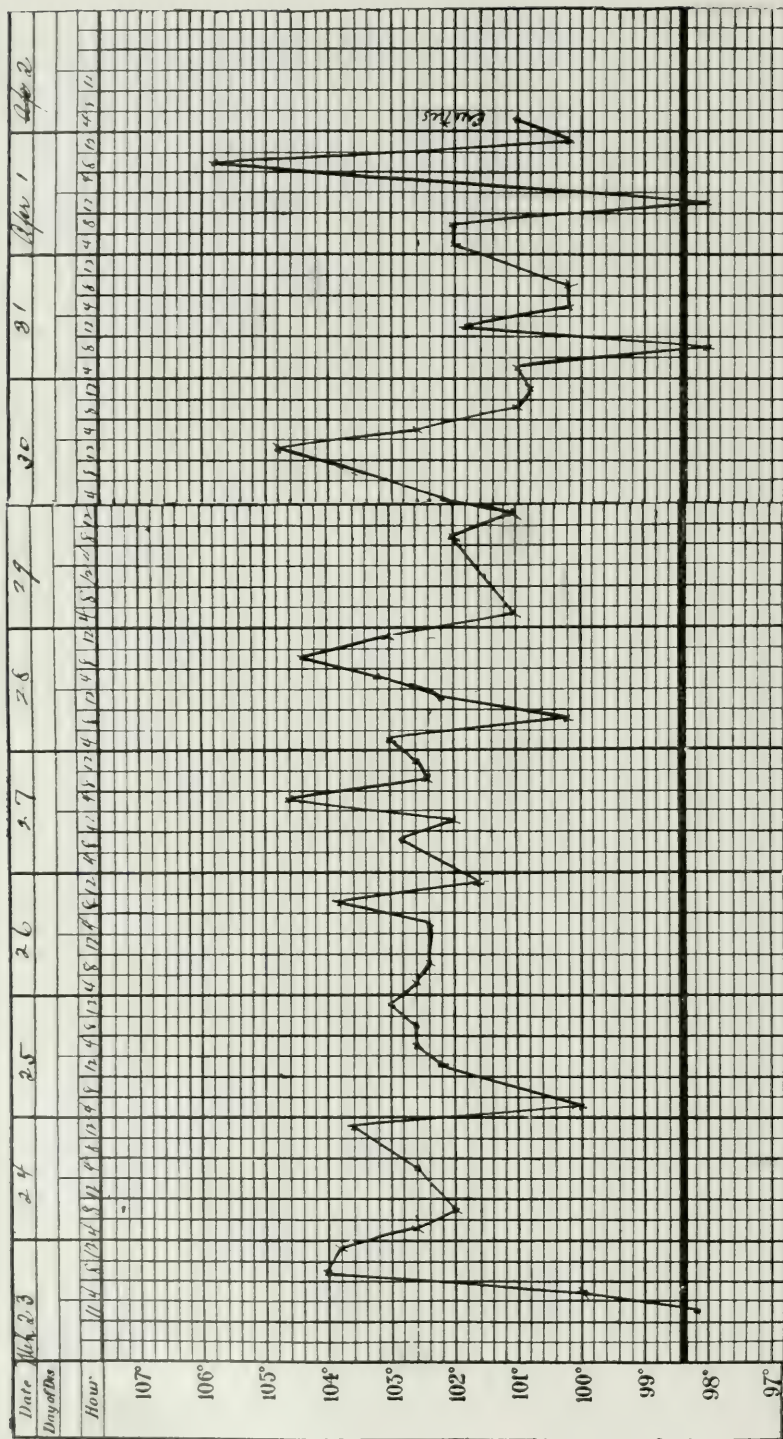


Fig. 2.—Chart showing temperature curve in Case 6.

was distinctly reddened and edematous. No pus was present in the nasal cavities. The tonsils appeared normal. The upper and middle lobes of the right lung crepitated rather feebly and the lower lobe was nearly airless. The pleura was everywhere smooth and glistening and in some places dark purple in color. On section the tissue was very moist and bloody, but no regions of consolidation appeared. From the bronchial tubes a frothy non-purulent fluid exuded on pressure. The lobes of the left lung also crepitated everywhere, though very feebly in the portions of the lower lobe, in which the tissue was dark red in color and soggy. The cut surface was moist and bloody, and from the smaller bronchi, on pressure, exuded a mucinous, slightly turbid fluid. No areas suggesting pneumonic consolidation appeared. The peribronchial lymph-glands were enlarged and dark red in color, without central softening or other change. The liver showed slight

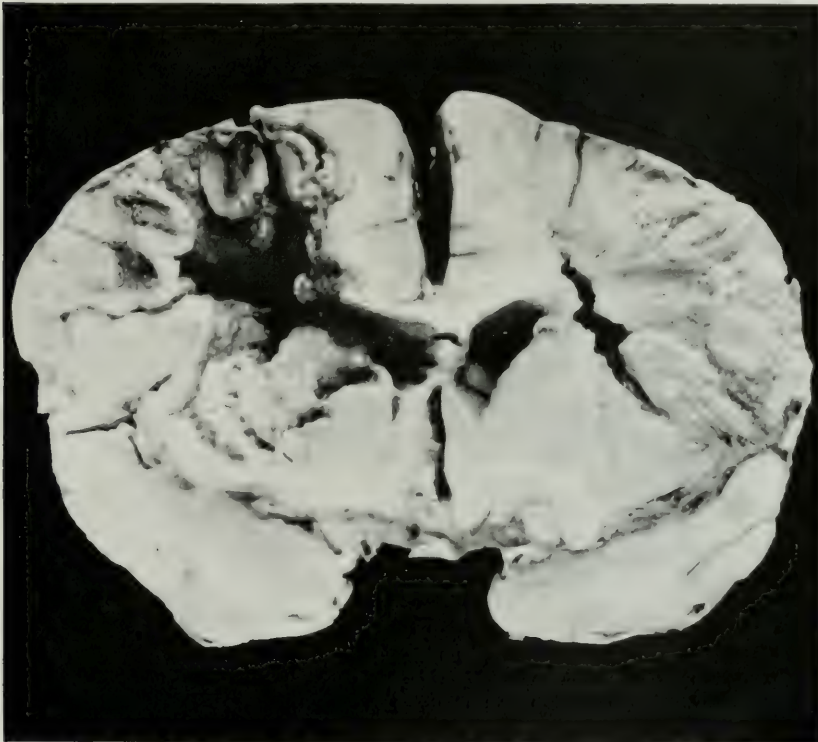


Fig. 3.—Photograph showing abscess formation in the left cerebrum in Case 6. Extensive softening of the cortex is also shown in the opposite hemisphere.

fatty change and the spleen was firm, swollen and had indistinct Malpighian bodies. The anterior fontanel tended to bulge slightly and the cerebrospinal fluid was increased in amount and was distinctly turbid but not bloody. Over the base and the surface of the brain, especially along the larger blood-vessels, was a thin, gray, fibrino-purulent exudate. The meninges were edematous and the convolutions were slightly flattened. The dura was deeply congested. In the meninges of the spinal cord a similar exudate was found. The tympanic cavities were both normal.

Microscopic Examination.—In sections through the cortex the exudate in the meninges was thin and composed almost entirely of polynuclear cells. In

places a few mononuclear cells appeared. The blood-vessels were intensely congested, but no hemorrhages were seen. Slight infiltration into the cortex of polynuclear cells occurred in places, especially along blood-vessels. Small bacilli were seen in the exudate. The exudate covering the cerebellum was more abundant, but was composed of similar cells. Extending along the spinal cord and enveloping the spinal roots was this same exudate, rich in polynuclear cells. The central canal was dilated and filled with exudate composed almost entirely of polynuclear cells. Little or no infiltration occurred in the surrounding tissue. In the lungs there was marked infiltration of round-cells, plasma-cells and leukocytes into the bronchial walls, with intense congestion of the blood-vessels. In the lumen were many polynuclear leukocytes. In the surrounding alveoli was a small amount of exudate containing some red cells and leukocytes. Marked edema occurred generally. Sections of the nasal mucosa showed marked infiltration, chiefly of round-cells into the mucosa, with congestion of the blood-vessels. Small areas of necrosis occurred in the centers of the Malpighian bodies in the spleen. The peribronchial lymph-glands, stomach, intestine, pancreas, adrenals, liver and kidneys showed no noteworthy changes.

Bacteriologic Report.—The cerebrospinal fluid, which contained a large number of polynuclear leukocytes and a few mononuclear cells in smear preparations, showed many small Gram-negative bacilli both within and without the leukocytes. In culture a pure growth of *B. influenza* was obtained from the exudate of the brain and the spinal cord. From the exudate of the left lung, which contained a considerable number of leukocytes, in culture were obtained many influenza colonies in symbiosis with the few pneumococcus colonies also present. Cultures of the heart's-blood also gave pure growth of the influenza bacillus. In the mucus scraped from the nasal mucosa a few colonies of this bacillus were obtained, and in addition many pneumococcus colonies. The pericardial and peritoneal fluids and the bile were sterile.

The homologous serum did not agglutinate the bacillus isolated from the heart's-blood, even in low dilutions. Growth from two pigeon-blood agar-slants introduced intravenously into a small rabbit produced no symptoms. The same amount injected intraperitoneally produced death in twenty-four hours and the bacillus was isolated pure from the peritoneal fluid and the heart's-blood.

CASE 5.—Infant, boy, aged 1 year. This case developed in St. Vincent's Infant Asylum. For some time there had been considerable "coryza" among the children, and several cases of bronchopneumonia, otitis media, etc., had developed. The nurses and attendants had been free from colds or "grip" infections. For several weeks previously the child suffered from bilateral otitis media and bowel disturbance, and became emaciated and anemic. Of late he was improving, when one week before death symptoms of bronchitis, fever and nasal discharge began, and later, evidence of bronchopneumonia. Five days before death meningeal symptoms appeared, manifested by rigidity of the back, neck and jaws, high fever, strabismus, moaning, etc.; a strong fetid odor from the nose and mouth was also noticed. Autopsy was made thirty hours after death.

Anatomic Diagnosis.—Acute purulent leptomeningitis; acute hemorrhagic pseudomembranous internal pachymeningitis; necrosis of nasal mucosa; bilateral purulent otitis media; bronchopneumonia; acute splenitis; parenchymatous degeneration of heart and kidneys; fatty liver; emaciation; strabismus; herpes labialis.

The child was emaciated. On the lower lip were small herpetic lesions. The anterior fontanel bulged slightly. The pupils were equal, moderately dilated and the left eye diverged. The sclerotics were pale and not icteric. In the pericardial cavity was about 20 c.c. of a clear, straw-colored fluid. Both lungs in the lower lobes showed small regions of pneumonic consolidation near the pleura on the posterior surface, which had a definite lobular distribution. In the bronchioles there was free pus. The upper lobes were normal. The lymph-glands about the hilus of the lungs were slightly enlarged. The liver was pale, rather soft and

in places light yellow areas were seen. The spleen was large, rather firm, brownish-red and the Malpighian bodies were indistinct. The kidneys were soft, large, and on section the tissue was swollen and dull red in color. The nasal mucosa was dark gray and covered by a thick, fetid, dirty, bloody membrane which extended downward into the pharynx and upward, where it could easily be traced, especially on the left side, to the cribriform plate. In the mouth, covering and adhering to the soft palate and also extending forward, was a bloody exudate appearing much like a blood-clot. The pharyngeal mucosa was red and covered with mucus; the larynx was covered with purulent mucus. The tonsils were not enlarged. In both tympanic cavities was a dirty looking pus but there was no evidence of invasion of the cranial cavity from these points. On opening the skull about a pint of bloody serous fluid escaped from the subarachnoid space. Lining the entire inner surface of the dura and slightly adherent to it was a definite fibrinous pseudomembrane, dark red in color, and 1 to 2 mm. thick (Fig. 1). This was not adherent to the pia. In the pia was an abundant purulent exudate which was bright red in color and distributed in patches, especially along the larger blood-vessels. At the base and beneath the frontal lobes the exudate was very abundant, and in this the olfactory lobes were imbedded. The cerebrospinal fluid was milky in appearance and had only the slightest tinge of blood. The purulent exudate extended downward into the meninges of the cord, but there it was not abundant. The bloody fibrinous pseudomembrane was also visible about the cord and extended to the cauda. The vessels in the meninges everywhere were deeply congested.

Microscopic Examination.—In sections of the cortex and pial exudate was seen an extensive infiltration into the meninges, consisting largely of polynuclear cells. There were a few mononuclear and plasma cells and here and there were considerable numbers of large endothelial-like cells often containing englobed leukocytes. In many of the small blood-vessels the lumen was filled with leukocytes, and occasionally the lining endothelial cells appeared swollen and cuboidal in shape. The walls were usually infiltrated with cells and thrombi could be seen in the vessels. The cellular infiltration into the cortex was very slight, there being only an occasional leukocyte seen, except along the small vessels penetrating the cortex from the pia where there could be seen, as a rule, a definite though not an extensive infiltration of round and polynuclear cells. Small hemorrhages occurred in this exudate. Distinct from this pial exudate was the extensive pseudo membranous exudate in contact with the inner surface of the dura. In sections the exudate was seen to be in intimate contact with the fibrous layers and was made up of an organizing layer containing round and elongated cells and some leukocytes. Fibrin was not abundant and in some places red cells were common. The dura itself was little changed. Sections of the cord made through the cervical portion and the cauda showed an extensive exudate, especially abundant about the nerve-roots, and there could also be seen in the cervical sections a layer lining the dura made up of red blood-cells, fibrin and leukocytes, which evidently corresponded to the cranial subdural exudate. This was also evident in sections through the cauda. The central canal contained an exudate consisting of leukocytes and round-cells.

In sections of the lung was seen a leukocytic exudate in the alveoli, especially those adjacent to the bronchioles. The latter were filled with leukocytes, and the walls were congested and infiltrated with cells, chiefly polynuclear and plasma-cells. Fibrin could be seen, but it was not abundant. The pleura was congested and in places covered by a delicate, fibrinous, cellular exudate. In the spleen were seen numerous areas of necrosis in which were round and lymphoid cells, and an eosin-staining homogeneous intercellular substance. These areas were definitely circumscribed and were located within or near the margin of the Malpighian corpuscles; no hemorrhages. Small hemorrhages occurred in the adrenal gland. The liver, pancreas, thyroid, intestinal mucosa, kidney, thymus and myocardium were not altered.

The cerebrospinal fluid, obtained at the foramen magnum, was milky in appearance and abundant. Cells were numerous and consisted of three varieties in the following proportions: Polynuclears, 66.4 per cent.; mononuclears, 30 per cent.; large endothelial cells, 3.6 per cent.

Bacteriology: In smears of the cerebrospinal fluid and the meningeal exudate were myriads of small Gram-negative bacilli both within and without the numerous polynuclear cells present. Cultures consisted of a nearly pure growth of *B. influenza*; a few large colonies, evidently of saprophytic bacilli, appeared also, and about them the influenza colonies were clustered. Anaerobic cultures of the exudate gave no significant organisms. In the middle ear were many streptococci and profusely growing saprophytes; no influenza bacilli. The heart's-blood, material from nose and other parts, contained such enormous numbers of saprophytic bacteria, probably post-mortem invaders, that the examination was unsatisfactory. No influenza bacilli were obtained in cultures of these fluids, though in smears Gram-negative minute bacilli suggestive of them were seen.

The growth from two small pigeon-blood-agar slants of the bacillus from the cerebrospinal fluid injected intraperitoneally killed a guinea-pig in eighteen hours and the organism was recovered from the heart's-blood and peritoneal exudate of the animal. A similar amount injected subcutaneously in a guinea-pig produced no symptoms. The bacilli were not specifically agglutinated by the homologous serum, even in low dilutions.

CASE 6.—Infant, girl, aged 10 months. One month before death the child caught cold and had some fever. Later she lost strength and weight, slept much of the time, and suffered from regurgitation of food. Ten days before death the child entered the Presbyterian Hospital, having marked rigidity of the neck and limbs; was in a stupor and unable to retain food. The anterior fontanel was bulging and eye symptoms were marked. Harsh breathing was present over the right upper lobe but there were no definite areas of dullness. Spinal punctures were made several times and a turbid fluid under pressure, containing many polynuclear leukocytes (90 per cent.) and Gram-negative small bacilli, was obtained. There was no growth in cultures on plain media. The temperature ranged from 100 F. to 104 F., as a rule, but on the day before death it dropped to 98 F., then suddenly rose to 105.8 F. (Fig. 2). The pulse was variable, usually ranging from 130 to 160 and the respirations ranged from 20 to 60. The leukocyte count was 21,050 and hemoglobin 80 per cent.

Autopsy.—Autopsy was held four hours after death. Anatomic diagnosis: acute fibrino-purulent leptomeningitis (influenzal); acute softening of right cerebral cortex; abscess in left cerebrum; internal hydrocephalus; bronchopneumonia; acute purulent bronchitis; fibrinous pleuritis; acute rhinitis; sub-pleural hemorrhages in right lung; petechial hemorrhages in skin; acute splenitis; septic infarcts in the spleen; fatty liver; acute degeneration of the kidneys and myocardium; localized fibrinous peritonitis; external strabismus; rachitis.

The anterior fontanel bulged slightly. On the abdomen, especially in the regions of the umbilicus and on the back were numerous small petechial hemorrhages, pin-point in size. There was no free fluid in the peritoneal cavity, but on the surface of the spleen and on the adjacent peritoneum were small gray flakes of fibrin. There was distinct enlargement of the juncture of the costal cartilages and the ribs. The tracheal mucosa was covered with a thin layer of grayish mucus which at the bifurcation was slightly purulent. In the lower lobes of both lungs, chiefly in the posterior portions, were consolidated areas showing a lobular distribution, and on pressure pus exuded in abundance from the bronchial tubes. Small pneumonic areas also existed in the upper lobes. The cut surface through the consolidated areas was dull gray, and as a rule mottled with red areas. In the pleura of the right lower lobe were small hemorrhages and over the consolidated portions the pleura was covered by a thin layer of fibrin. The peribronchial lymph-glands were large, soft and pink; no necrosis. The heart, thyroids and thymus were unchanged.

The spleen was large, firm and purplish-red in color and portions of the capsule were covered by a thin layer of grayish-yellow fibrin. The cut surface was red and the Malpighian bodies were small and indistinct. Along the anterior margin under the capsule were a number of small, yellow, soft areas 2 or 3 mm. across, which involved the substance of the spleen to a depth of 2 mm. or more. These areas appeared necrotic, but no pus exuded on section. The liver was soft, yellowish-brown in color and the lobules were very indistinct. The kidneys were soft, markings indistinct, and on section the cortex appeared pale and swollen. The remaining viscera showed no noteworthy changes.

On opening the cranial cavity a large amount of turbid cerebrospinal fluid was encountered. The brain was very soft and everywhere there was an abundant greenish-yellow, highly purulent exudate. This was especially abundant along the larger vessels and along the base. Over the hemispheres it was arranged in patches or islands surrounded by relatively clear meninges. The convolutions were flattened, especially in the frontal lobes and at the base. The brain, on section, showed an extensive area of softening involving the right cortex from the median fissure to the Sylvian fissure, chiefly in the Rolandic area. On the opposite side an abscess (Fig. 3) containing a large amount of greenish-yellow pus was found just below the surface and extending down to and into the lateral ventricle. There was no definite wall, the tissue at the margin being soft and necrotic. No definite hemorrhages occurred. Distinct dilatation of the ventricles was present especially evident in the fourth ventricle. The exudate extended throughout the spinal canal, but there it was less abundant than in the cranial cavity. The meninges were intensely congested everywhere. The cranial dura was red in places and here and there thick green pus adhered to its inner surface. The tympanic cavities appeared normal. There was a small amount of gray, purulent mucus in the nasal cavity, and the mucosa was smooth, but slightly reddened, and was covered by a thin layer of mucus; no necrosis.

Microscopic Examination.—In the lungs the bronchioles showed intense inflammatory changes, consisting of degeneration of the epithelium, and congestion and marked infiltration of plasma-cells in the submucosa. Polynuclears were abundant in the lumen but rare in the submucosa. The alveoli contained many polynuclear leukocytes, and in places a small amount of fibrin. In sections through the softened portions of the brain could be seen many bacterial emboli in the small blood-vessels. The bacteria resembled influenza bacilli and were largely confined to the vessels. Very slight infiltration occurred in the surrounding tissue, which stained poorly. No definite abscess wall was visible. The meninges showed intense congestion and infiltration, chiefly with polynuclear cells.

Bacteriology.—In the purulent exudate from the surface of the brain and in the cerebrospinal fluid were myriads of minute Gram-negative bacilli which on culture proved to be *B. influenzae*. They also occurred in large numbers in the bronchial pus, but were not isolated in culture from the other body fluids, though in smears of the nasal exudate numerous small Gram-negative bacilli were seen. In the meningeal and bronchial pus there were also a few streptococcus colonies on the blood-plates and this organism was also found pure in the heart's-blood and pericardial fluid and mixed with saprophytic bacilli in the nasal cavity.

One c.c. of the greenish pus from the cortex was injected subcutaneously into a guinea-pig. On the following day the animal appeared inactive and later lost some weight; after a few days it had entirely recovered. A second pig was injected with one pigeon-blood agar-slant culture intraperitoneally. Death followed in twenty-four hours, there being edema of the abdominal wall and marked peritonitis. The bacillus was recovered from the heart's blood and the peritoneal fluid.

Agglutination experiments using the homologous serum were negative.

CASE 7.—Infant boy aged six months. Forceps delivery at 8 months; child in good health until the present illness. Feb. 17, 1910, the child was taken sick with vomiting and fever (102.5 F.), and the mother noticed a peculiar

quivering of the chin. During the night he moaned almost constantly and the next morning (February 18) appeared sick, pale and waxy. In the afternoon several convulsions occurred. At this time the child was unconscious, the neck was rigid, the pupils did not react to light and there were twitchings of the left side of the face, angle of mouth and the left hand and foot; both limbs on the left side were rigid and Kernig's sign was absent. There was slight dulness over the right lung posteriorly. Spinal puncture gave an abundant turbid fluid, which contained a large number of cells, nearly all of which were polynuclear leukocytes. There were also present many very small Gram-negative bacilli, mostly extracellular, but some definitely intracellular. They were distinctly polar-staining, and occasionally thread-like forms appeared. They failed to grow on plain media. Morphologically these bacilli were typical *B. influenzae*. Unfortunately the cultural properties were not studied, as blood media were not inoculated. Two injections of 25 c.c. each of Flexner's serum were given without result. The child gradually became worse and died February 20, three days after the initial symptoms began. No autopsy.

GENERAL CONSIDERATIONS

These seven cases of influenzal meningitis occurred in Chicago in the course of little over a year, all resulting fatally, and in duration varying from three to fourteen days. All were infants, the oldest being 13 months and the youngest (twins) 5 days old. A definite history of colds preceding the meningeal trouble, as a rule, several weeks, was obtained in four cases. The occurrence of the disease in the twins, beginning simultaneously, is suggestive of a common source of infection, but in this instance it could not be determined. Cases 3 and 4 came from a small institution¹⁰ for children in which an epidemic of "colds" had existed for several weeks. The children were all in intimate contact constantly with each other. In Case 4 the patient developed the disease about four weeks after the child in Case 3 was taken ill, or about two weeks after her death. A few days after the death of Patient 4, and while a number of the children were suffering from colds, though not severely ill, swabs were taken from the noses and throats of all the children (twelve cases) and examined in smear and by pigeon-blood agar-plates for influenza bacilli. The results were negative in all cases. *Streptococcus pyogenes* was numerous and generally was the predominating organism in all cases. Staphylococci and pneumococci were also common. Case 5 also developed in an institution for children at a time when many cases of "colds," and especially bronchopneumonia were occurring there. The children did not come from the poorer parts of the city, and, excepting the association of Cases 1 and 2 and Cases 3 and 4, no relation could be ascertained. Cases 1 and 2 developed in October, 1908; the others occurred in the winter months of 1909-1910, during which period a general influenza epidemic was not raging.

10. This institution is conducted by Dr. Effa Davis, to whom I am indebted for the opportunity to examine the cases bacteriologically.

As a rule the onset in these cases was indefinite and the exact time when the meningeal trouble began could not always be determined. Eye symptoms were usually present and in all cases rigidity of the back and the limbs and retraction of the head were marked. Definite convulsions occurred in five cases. Other early symptoms were cough, harsh breath-sounds or definite signs of pneumonia, bowel disturbances and restlessness. Bulging of the fontanel was evident in all cases and herpes labialis was present in one case. Small petechial hemorrhages in the skin occurred in Case 6 a short time before death. The temperature generally was variable, ranging from normal to 105 F. or higher, and subject to sudden change (Fig. 2). The pulse was irregular but usually rapid (130-160). The period of incubation cannot be over five days, since the twins became ill on the fifth day after birth.

Lumbar puncture was made in four cases and in all there was obtained a turbid fluid, under high pressure, in which were many leukocytes, the polynuclear cells always predominating. Differential counts gave from 60 to 80 per cent. polynuclear cells, the remainder being chiefly small mononuclear cells. Endothelial cells were also commonly found. Red cells were not found, or occurred in small numbers and the fibrin was scant.

Five of the seven cases were examined post mortem. An abundant, highly purulent, greenish-yellow leptomeningeal exudate was found in four; in the remaining child (Case 4), which died on the third day, the exudate was less profuse and limited chiefly to the base and the vessels in the Sylvian fissure. Generally the exudate was very abundant at the base and about the frontal lobes and in these regions marked compression of the convolutions occurred. Often the exudate over the cortex was distributed in large patches and usually was much more abundant along the blood-vessels. In one case (Case 5), delicately attached to the dura, was an extensive hemorrhagic exudate which, after hardening, closely simulated a definite membrane. This was entirely independent of the purulent pial exudate, from which it could readily be separated. On microscopic examination this exudate was found to consist of red-cells and layers of fibrin, together with an infiltration of leukocytes and fibroblasts. In sections of the spinal cord, even at the cauda, this membrane was observed on the inner surface of the dura and independent of the more purulent exudate involving the pia-arachnoid. Exudates of this type have not been reported in influenzal infections of the meninges, though similar changes have been described in connection with meningococcus infections. In all cases the dura was red and congested and usually some of the greenish, thick pus adhered at the base after removing the brain. In Case 6 a very extensive softening containing thick greenish-yellow pus in which were bacilli in abundance formed under the cortex

and penetrated the lateral ventricle. This is the first case of this disease in which a cerebral abscess has been noted. On the opposite side of the brain was extensive softening of the cortex, but no definite abscess formation.

In none of the cases did hemorrhage into the brain substance occur. Acute hydrocephalus was marked in Case 6, a condition noticed by others in influenzal meningitis, and also not a rare occurrence in other forms of meningitis.

The spinal cord was removed in four cases and in general the exudate here was less in amount than in the cranial cavity. Usually it was more abundant on the posterior surface and was profuse in the pia-arachnoid and about the nerve-roots. Often the infiltration penetrated the substance of the cord, especially along the blood-vessels, and could be traced well into the gray matter. Pus was seen in the central canal of the cord in two cases (Cases 4 and 5).

Histologically the exudate was extremely rich in cells, and fibrin was absent or present in traces, so far as one could tell from the formalin-fixed preparations. The cells were of three types, namely, polynuclears, mononuclears and large endothelial-like cells. In certain areas the exudate was composed almost exclusively of polynuclears; in other parts mononuclears and the endothelial cells were common. The latter often had from one to three polynuclear or mononuclear cells included in their protoplasm. These cells appeared to be the desquamated endothelial cells which line the arachnoid spaces, which have been noted in meningococcic meningitis, especially by Councilman. Sections stained for influenza bacilli revealed the organisms in the exudate. Small hemorrhages were sometimes seen in the exudate and the blood-vessels at times were thrombosed and the walls infiltrated with cells. Always the exudate followed the pia into the deepest sulci and often extended for a short distance along the vessels into the cortex. The infiltration of the cortex, however, was generally not extensive and excepting the softened areas and abscess in Case 6 it was limited to the occurrence of a few polynuclear and plasma cells near the surface.

In one case bilateral purulent otitis media had been present for several weeks. Acute rhinitis was found in three cases, one (Case 5) showing extensive necrosis of the entire nasal mucosa, involving the cribriform plate and extending downward into the pharynx. The tonsils were slightly enlarged in two cases. Acute bronchitis was present in four and bronchopneumonia in three cases. The pneumonic consolidation, as a rule, involved the posterior portion of the lungs and was more extensive in the lower lobes. It was distinctly of the lobular type and the infiltration about the bronchioles in the peribronchial lymph-channels was characterized by the presence of large numbers of plasma cells. As a rule

few polynuclear cells appeared here. Fibrin was scant, though in places it was definitely visible. The exudate in the bronchial tubes and in the alveoli contained chiefly polynuclear and desquamated epithelial cells.

In no instance was there effusion into the pleural cavities, but in three cases, in which bronchopneumonia existed, the pleural surface over the involved regions was granular and lusterless. In Case 6 there was a marked though not extensive fibrinous layer covering the pleura and beneath were numerous small but definite hemorrhages. In this connection may be mentioned the hemorrhages on the surface of the thymus in Case 1, and the petechial hemorrhages in the skin in Case 6. In all cases the liver presented evidence of fatty change. Icterus was not noted.

It was common to find a small amount of slightly turbid fluid in the peritoneal cavity. In Case 1, influenza bacilli were obtained in considerable numbers from this fluid but there was no macroscopic evidence of peritonitis. In Case 6 on the spleen and regional peritoneum was a definite gray, fibrinous exudate originating and extending from the infarcted areas in the spleen. The adrenals showed no noteworthy change in any case. Generally, acute degeneration of the various viscera was evident.

The various fluids of the body collected at autopsy were studied bacteriologically in smear preparations and on pigeon-blood agar-plates. The influenza bacillus was isolated in practically pure culture from the meningeal exudate and cerebrospinal fluid in all post-mortem cases. They were present usually in enormous numbers, as shown by the smear preparations, and were always both within and without the polynuclear cells. In two cases (3 and 4) they were found pure in the heart's-blood in large numbers. In both these cases the autopsy was held while the body was still warm; consequently there can be no doubt that the bacilli were present in the circulating blood before death and might have been isolated by blood-cultures, had such cultures been made. In one case the bacilli were found in the peritoneal fluid and once in the pericardial fluid. In three cases they occurred mixed with streptococci in the bronchial secretions, and once they were grown from the surface of the nasal mucosa. On account of the difficulty with which this organism sometimes grows it is possible that its distribution was more general than the positive cultures indicated. In smears from the nose Gram-negative minute bacilli were found in two cases, which were not recovered on the plates. In Case 5 in which there could be no doubt that the infection invaded the cranial cavity through the cribriform plate from the nasal cavity, no influenza bacilli were recovered from the nasal exudate, probably on account of the presence of large numbers of other organisms. In Case 6 a terminal streptococcus infection occurred, these organisms being found in the heart's-blood, pericardial fluid, nasal exudate and bronchial pus. A few were also found in the meningeal exudate, but in insignificant num-

bers compared with the influenza bacilli, myriads of which, in symbiosis, were crowded around the streptococcus colonies. That the streptococcus was a terminal infection is evidenced by the fact that this organism was not found in culture of the spinal fluid obtained by lumbar puncture before death.

The atrium of infection was not certain in all cases. In Case 5 the infection could be traced directly from the nasal cavity through the necrotic cribriform plate. In Case 4 the bacilli were found in large numbers on the inflamed nasal mucosa, and in Cases 3 and 6 the infection probably originated in the upper respiratory passages. Four of the cases had bronchitis or pneumonia, from which lesions the bacilli were isolated. From the clinical data, however, one cannot be certain whether or not these lesions antedated the meningitis. In Case 1 gastro-enteritis was present at autopsy, symptoms of which appeared at the onset. The massive meningeal exudate under the frontal lobes and at the base of the brain in all cases points rather strongly to a nasal origin, and the fact that generally these cases had been troubled with infections of the upper respiratory tract would seem to substantiate this idea.

Morphologically and biologically the influenza bacilli isolated in these cases were in no way different from bacilli commonly found in sputum in various infectious diseases. They were very minute, Gram-negative, distinctly bipolar when stained, and susceptible to phagocytosis. In smears of the meningeal pus one occasionally saw some tendency to form threads, this being most marked in Case 7. In cultures, as a rule, this tendency was greater, not infrequently long and curved thread-forms being common. In the culture from Case 6 this was especially noted, and at times growths were obtained which were made up largely of long threads resembling a leptothrix. The colonies of the various strains presented the typical dew-drop appearance, were not hemolytic, and grew only in hemoglobin media, with a preference for pigeon-blood-agar.

The property of symbiosis was marked in all strains. Attention should be directed to this very important characteristic, which serves to distinguish this organism from other closely related bacilli. Advantage was taken of this property in the examination of the various fluids by purposely contaminating the plates or media with other germs. In some instances positive influenza cultures were thus obtained about the foreign colonies when growth was not evident in the uncontaminated cultures. It is therefore advisable at times to thus purposely contaminate the media, using of course proper controls, when searching for this bacillus in spinal fluid, blood, and other fluids.

Serum was obtained from the heart's-blood in four cases and its agglutinating power tested, using the homologous bacilli, and also bacilli

from other cases. The results were negative. Both macroscopic and microscopic methods were used.

The bacilli isolated post mortem were all tested on guinea-pigs or rabbits with the following results: injected into the peritoneum of guinea-pigs, growth from two small agar-slants caused death in twenty-four hours. Subcutaneously this amount was not sufficient to cause death. Several drops of thick pus from the meninges intraperitoneally in guinea-pigs was not sufficient to cause death. Compared with bacilli from sputum of other cases they appear to have about the same degree of virulence. All strains were quite similar in their pathogenicity and could not be called highly virulent for the animals tested.¹¹

I am indebted to Dr. F. S. Churchill for the clinical reports in Cases 1, 2 and 7, and to Dr. Effa Davis for the clinical records of Cases 3 and 4. Case 5 developed in St. Vincent's Orphan Home in the service of Dr. Baxter, and in Case 6 the patient entered the Presbyterian Hospital in the service of Dr. Cotton.

11. Cohen (see note 3) found that the bacilli from his cases were highly virulent for animals, tending to produce a rapid and fatal septicemia. On this fact, and also on certain facts obtained with the agglutination reaction, he attempted to differentiate these meningitic bacilli from the true Pfeiffer's bacillus. It is probable that he was dealing merely with a more highly virulent influenza bacillus.

OBSERVATIONS ON THE TREATMENT OF CHRONIC INFANTILE PARALYSIS

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The triumphant event in the study of chronic infantile paralysis is the change in the minds of the profession toward a more favorable prognosis. Whereas only a decade ago the accepted verdict was that "muscles which do not recover in the first weeks or months usually remain paralyzed for a whole life time" (Strümpell), now the belief is that "treatment faithfully and persistently continued is frequently rewarded by the return of power and usefulness in the atrophied and helpless limb" (Young).

Coupled with this change is the growing confidence in the simpler forms of treatment for this disease. For instance, it has but recently dawned on orthopedists that in tendon transplantation the benefits derived were due to the persistency of the after-treatment rather than to the substitution of a healthy tendon for a degenerated one. In the Hospital for Deformities and Joint Diseases of the City of New York, where approximately 1,100 cases of chronic infantile paralysis were treated within the last four years, the methods used were as follows:

Scarcely any tendon transference, arthrodesis, tenodesis, or nerve-grafting were done, while operations were limited only to the correction of paralytic deformities. Braces were avoided as much as possible, because of their tendency to lull the parents into the false belief that the child was wearing something which would cure him, and thus tend to make them neglect the treatment. Hand massage, the interrupted galvanic, the faradic and the sinusoidal currents were used. Practically all cases, not only those in the recession stage, in which improvement is physiologic, but those also in which the paralytic attack was of over a year's duration, improved under this treatment. This is especially so in those cases in which previous treatment was neglected or imperfectly carried out.

EFFECT OF MASSAGE IN INFANTILE PARALYSIS

Sometimes a child suffering from this disease cannot contract a muscle or a group of muscles, not because they are paralyzed, but because they are inflamed. When this is the case the child winces or cries with pain when the muscles are massaged, while palpation of these muscles elicits tenderness. This tenderness is caused by the hyperstretching of the paralytic muscles, which injures the contractile element and produces

a myitis or an actual neuritis. Massage helps to overcome the inflammation and voluntary motion is possible.

Straining the ligaments of the joints is common in infantile paralysis, because in urging the child to walk, his weakness produces abrupt movements which cause strain. Paretic muscles are also incapable of much exertion. In exercising these patients we are apt to overwork them, which causes stiffness of the muscles the next day, so that often patients cannot do their exercises as well as they did at the previous treatment. Massage helps to relieve the sensitiveness of the muscles and ligaments, which is caused by the above strain and fatigue.

The hardest part of the exercises occurs at the beginning when the child has to overcome the locking of the muscles. This locking of the muscles is produced by the hyperstretching of the paralytic group and the contracting of their opponents. Massage stimulates the contractile element of the stretched muscles and tends to relax the spastic opponents. It also raises the temperature of the muscles. This raised temperature, usually from 1 to 5 degrees Fahrenheit, renders the muscles electrically susceptible, i. e., it takes a smaller amperage to cause contraction of paretic muscles after massage than before. The importance of this phenomenon from a therapeutic standpoint is self-evident.

The belief that massage builds up atrophied muscles I find to be incorrect. In the Lucas-Championnière method for the treatment of fractures, in which the limb is thoroughly massaged daily, massage diminishes but does not prevent the atrophy of muscles. Nor does massage and electricity prevent atrophy of inactive muscles. I have tried this a number of times on limbs that were held by posterior splints for inflamed joints. Despite the daily use of massage and the interrupted current, flabbiness of the muscles appeared in a short time. If, therefore, massage or the use of massage and electricity do not prevent the atrophy of healthy but inactive muscles, these agents certainly cannot "build up" atrophied and partly degenerated muscles, such as exist in chronic infantile paralysis.

Atrophy seems to be the result of the law of supply and demand of the organism, which is, that increased function of tissue is followed by the increased size and strength of the tissue; diminished function by atrophy, and useless tissue by degeneration. The lesion in chronic infantile paralysis is a destruction of motor cells in the spinal cord, while the part of the cord affected is shrunken and sclerotic. Improvement in the chronic stage is not due to the regeneration of motor cells in the spinal cord. The pathologic law that dead organic cells never regenerate is fixed. Improvement is due to the physiologic law that cells increase in size and strength with function, and that sometimes a cell takes over to itself the function of the destroyed neighboring cell. This must be true. How else can we explain the improvement that takes place in the chronic

stage of this disease and the fact that many children gradually outgrow their trouble?

In order to understand the *modus operandi* of the treatment in the chronic stage of this disease, we must first glance at the structures that are involved in a voluntary muscular contraction. They are, the motor cells in the spinal cord, the spinal nerves, the muscles, the conducting tracts, the motor centers in the brain, and the will power. In chronic infantile paralysis there is a break in this psycho-neuro-muscular cycle at the motor cells in the anterior cornu of the gray matter of the spinal cord. Atrophy and degeneration in chronic infantile paralysis is not only limited to the muscles, but also affects the nerves, the conducting tracts and the motor cells in the brain centers dominating the affected muscles, and the will power to concentrate on these brain centers becomes weakened from disuse caused by the break in the cycle.

Since the contractile element of the muscles is often injured or destroyed by the hyperstretching of the paralyzed muscles or by atrophy and degeneration, it is obvious that the care of the muscles themselves is imperative in this disease. Massage and electricity exercise the muscles, but the exercise produced by these agents is of a passive variety (an exercise of muscles without the exercise of the other structures of the cycle), and clinically we know that the benefit of passive exercise is slight. Permanent benefit is only derived from the simultaneous and coordinated exercises of all the elements of the cycle. This is only possible during voluntary muscular contraction, because in this wise the will power and the atrophic brain cells are exercised and by reciprocal action the motor cells in the spinal cord are developed and the muscles strengthened. And so, at bottom, it is the exercise of the will power that causes improvement in chronic infantile paralysis, by developing the gray matter in the brain and cord.

The dominant effect of massage is suggestion. The suggestion of massage in chronic infantile paralysis differs, however, from the psychic effect that massage has on the adult patient in other diseases. In the adult patient massage makes him feel that he is being "benefited," an element in massage long recognized, which explains its popularity in the treatment of nervous diseases. In chronic infantile paralysis in children, however, massage suggests focusing their will-power on the motor brain centers of the affected muscles and stimulating them into action. Suggestion itself, however, may not produce the desired effect or may even produce an opposite effect, which is true oftentimes of suggestion in general as, for instance, when a physician suggests or tells a neurasthenic that he is free from organic diseases and that he will get well, the patient becomes convinced that the opposite is true. Resistance to suggestion or command is often observed in the beginning of treatment of children with

chronic infantile paralysis. The strange surroundings of the dispensary or office, the manipulations, etc., frighten the child and arouse its antagonism, so that the child persists in contracting the muscles under massage and suggestion, or command to contract the paretic muscles is followed either by no response at all or only by desultory and superficial contraction.

The masseuse, however, towers over the child, grasps the limb with one hand and with the other executes movements on the body of the child which are centripetal or circular and which induce a tingling and a thrilling sensation. These movements are monotonous and are made in front of the child and resemble the passes of a hypnotist. I have seen children who when first massaged were unhappy and cried, but later become used to it and lie during the treatment completely relaxed with flushed faces and dreamy looks, a condition resembling the prehypnotic state in which the mind becomes susceptible to impressions. These various manipulations (rubbing, kneading, striking, etc.), performed during that period are suggestions to the child to contract the involved muscles. These suggestions repeated so frequently accumulate into a hypnosis which arouses and concentrates the child's will power on muscular contraction.

We see this often, in fact, when children who at the beginning of the treatment respond feebly to the command to contract their muscles, later begin to focus their energy to such an extent that their faces are flushed from the exertion. These extreme efforts can hardly be explained by the theory of the child's own initiative, but are rather prompted by a hypnosis which resulted from the movements of the masseuse.

PASSIVE MOTION

In passive motion the masseuse relaxes the stretched muscles and stretches the contracted ones. This is temporary, however, as the muscles slip back to their former position as soon as the hand of the operator is removed. During passive motion no muscular contraction takes place, and the effect, therefore, of these movements on the muscles themselves are practically nil. Its value is chiefly due to the fact that during the relaxation of the stretched muscles and the stretching of the contracted muscles such movements are suggested to the child.

ELECTRICITY

"Except as a matter of exercise, electricity is practically useless" (Sachs). The interrupted currents exercise the muscles and hinder the atrophy and degeneration which progress in the muscles. The exercise, however, induced by the currents is of a passive variety, since it affects the muscles alone, and the benefit of such exercise is slight. We see

cases in which a group of muscles have regained their power (as shown by their response to the faradic current), and still the child is unable to contract them. This can be accounted for by the child either forgetting how to contract the muscles during the period of their inactivity, or by his will-power to concentrate on these brain centers becoming weak from disuse. I believe that the chief value of the interrupted currents is not due to their local effect on the muscles, but is due to the impulses of the muscular contractions that are conveyed and registered on the child's brain. These impulses are object lessons to the child which imperatively suggest imitation of the movements.

CONCLUSIONS

The benefits of massage, electricity and passive motion are not due to the local effect of these agents on the muscles. In chronic infantile paralysis the affected muscles are unbalanced, atrophied and partly degenerated, are subnormal in temperature and have subjective symptoms of weakness, stiffness in exercise, and often of pain. The above agents, especially massage, relieve the pain by their counter-irritating effect, and the stiffness by their antispasmodic action, and temporarily raise the temperature and relieve the weakness by exciting the circulation and stimulating the contractile element in the paretic muscles. These effects help the patient to bring the muscles under the control of the will-power and facilitate their exercise. The chief value of these agents, however, is due to their reflex mental action, consisting of suggestions, of impulses of muscular movements which are conveyed to the brain, and which the child instinctively imitates, and the building up of an hypnosis which arouses the mental energy of the patient into a concentrated effort during the muscular contractions.

That this is true is proved by observations in the gymnasium. A bright child, for instance, a type generally susceptible to impression, makes greater progress during the treatment than the stupid child, a type not susceptible to suggestion. No matter how much local treatment the latter receives, he remains unresponsive and makes little progress. It is also proved by cases in which physicians have given a great deal of local treatment, together with a bad prognosis, and the patient has made but little progress during that time. Finally, perhaps, an intelligent parent or nurse may have applied herself with energy to the treatment of the child and produced remarkable results in a short time. Instances of that kind are not at all rare, and reports of such occurrence have of late found their way into the lay press.

The prime factor in these "miracles" has been the enthusiasm for work aroused in the child. In most of them very little local treatment was used, and it was mainly limited to massage. The form of massage

employed consisted generally of upward and downward strokes, the effect of which was to stimulate the nerve endings and draw the blood temporarily to the surface. Such massage, which is conspicuous for its flagrant disregard of all the principles of scientific massage, has little effect on the muscles themselves. Its reflex mental effect on the patient, however, is tremendous. It is practically the fetish which creates the enthusiasm. It is the carrier of the hypnotic impulses that arouse the will power to concentrate to the utmost during the muscular contractions, and which leads to the building-up of the mental and motor brain-cells.

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A STUDY OF BLOOD-PRESSURE IN NORMAL CHILDREN

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It was 100 years after Harvey's discovery of the circulation of the blood that Hales demonstrated blood-pressure (1733), but it was a century later before physiologic experiments gave any reliable results. Ludwig¹ in 1847 was the first to obtain a blood-pressure tracing, by means of a recording manometer directly connected with an open artery. These experiments quickly led to the introduction of clinical methods. V. Basch in 1882 constructed the tonometer, the perlotte of which could be placed over any artery. Roy and Adami² in 1890 constructed the first instrument based on direct compression of the artery—a flexible rubber bag containing water to exert the pressure and a mercurial manometer for a recorder. In 1896 Riva Rocca and Leonard Hill independently substituted air for water in the bag for compression and, although a number of other instruments have since been invented, the Riva Rocca model is the one which has proved most practical for general use.

V. Basch³ as early as 1894 advised sphygmomanometry in children, and took the pressure with his tonometer in sixty-eight children in Monti's clinic in Vienna. In 1893 Friedman⁴ took the blood-pressure of a number of children in Heubner's clinic, but drew no definite conclusion. The first important work was done by Oppenheimer and Bauchwitz⁵ in 1905 and was followed by Eminent's⁶ in 1907 and Seiler's⁷ and Wolfensohn's⁸ in 1910.

Age is the factor on which the standard of blood-pressure has always been based, but the normal limits have varied greatly according to different observers. In infants the pressure ranged from 75 to 90 mm.; in children over 2 years from 90 to 115 mm.; in young adults from 115 to

1. Janeway: *The Clinical Study of Blood-Pressure*, 1904.

2. Oliver, G.: *Studies in Blood Pressure*, 1908.

3. Von Basch: *Ueber Pulse Fuehlen, Pulse Schreiben, und Pulse Messen*, Arch. f. Kinderh., v, 7.

4. Friedman: *Jahrb. f. Kinderh.*, lxiii-lxxxv.

5. Oppenheimer and Bauchwitz: *Ueber den Blutdruck bei gesunder Kinder*, Arch. f. Kinderh., 1905, xlii.

6. Eminent: *Sphygmographie und Tonometrie bei gesunder Kinder*, Arch. f. Kinderh., 1907, xlv.

7. F. Seiler: *Ueber den Blutdruck im Kindesalter*. Cor.-Bl. f. Schweiz. Aerzte, May 10, 1910.

8. Frau Wolfensohn-Kriss: *Ueber den Blutdruck im Kindesalter*. Arch. f. Kinderh., liii, Nos. 4-6.

130 mm. H. W. Cook⁹ who investigated the value of the blood-pressure as a guide to stimulation in sick children, says that normal pressure in children varies rather widely because of many factors, including height, weight, and size of the arm, and although such a pressure may be called high for a child of a certain age, and another low, each reading must be judged by the circumstances of the case. Cook, however, did not attempt to find any relation between these factors. In fact, no one did until Frau Wolfensohn⁸ in 1910 studied the relation between height and weight and blood-pressure. She draws the following conclusions from the study of 350 children:

1. Blood-pressure increases with age.
2. Blood-pressure increases with height and weight.
3. Children of the same age but of different weights and heights have different blood-pressures.
4. Sex is of no importance. Boys and girls show the same blood-pressure if their heights and weights are the same.

In the following study I have taken not only the weight and height into account, but also the circumference of the arm and have, according to Sallom's¹⁰ method, in adults, estimated the pressure per square millimeter in the hope of obtaining a more accurate standard for normal children. I used Cook's modification of the Riva Rocca instrument with a cuff of 9 cm. width. I did not forget von Recklinghausen's¹¹ observation that errors are frequently due to a too narrow armlet, and that one narrower than 10 cm. should never be used. However, in the examination of a number of children it was found that the readings averaged only 5 mm. lower with the wider than with the narrower cuff, which is much more easily adjusted on their small arms. The children were seated at a low table, the cuff smoothly adjusted around the arm and connected with the mercurial manometer. Pressure was exerted until the pulse disappeared, then greater pressure was exerted until the mercury was far above the point of disappearance of the pulse. It was then allowed to drop until the pulse was again palpable. The point of disappearance and reappearance usually corresponded, and registered the systolic pressure.

In all, 128 normal children were examined, some several times to gauge the accuracy of results. The readings were taken as nearly as possible at the same time of day and under the same conditions, and the height, weight, and arm circumference measured. First, as to weight and height, just as in Frau Wolfensohn's experience, it can be seen from

9. Cook, H. W.: Clinical Value of Blood-Pressure Determinations as a Guide to Stimulation in Sick Children, *Am. Jour. Med. Sc.*, 1903, p. 483.

10. Sallom, A. K.: Standardization of Blood-Pressure. *New York Med. Jour.*, Sept. 24, 1910.

11. Von Recklinghausen: *Arch. f. Exper. Path u. Pharm.*, 1902, xlv, 78.

the following tables that there was apparently an increase in pressure with the increase in height and weight.

TABLE 1.—COMPARISON OF HEIGHT AND SYSTOLIC BLOOD-PRESSURE

Height.	Systolic
	Blood-Pressure. Mm.
3 ft. 6 in.	99
4 ft. to 4 ft. 3 in.	109
4 ft. 3 in. to 4 ft. 6 in.	112
4 ft. 6 in. to 4 ft. 9 in.	118
4 ft. 9 in. to 5 ft.	120
5 ft.	125

TABLE 2.—COMPARISON OF WEIGHT AND BLOOD-PRESSURE

Weight, Pounds.	Blood-Pressure, Mm.
30 to 40	95
40 to 50	100
50 to 60	107
60 to 70	112
70 to 80	116
80 to 90	122
90 to 100	126

I say apparently, for, when the circumference of the arm is measured and the blood-pressure per square millimeter is estimated, according to Sallom's¹⁰ method, it is seen that the actual blood-pressure is practically the same for a 5-year-old child of 3 ft. 6 in., weighing 40 pounds, and a 15-year-old child of 4 ft. 8 in. weighing 90 pounds.

In a recent article on blood-pressure in adults A. K. Sallom¹⁰ says that the area on which the pressure is exerted must be considered in estimating blood-pressure, for it is a law of physics that pressure exerted by any fluid depends on the height and width of the base. The actual blood-pressure then must equal the height of the mercurial column, divided by the width of the cuff, multiplied by the circumference of the arm. For example, A. K., blood-pressure 120 mm.; arm circumference 183 mm. $\times$ 90 mm., the width of the cuff equals 16,470 square mm.; then if 16,470 square mm. will sustain 120 mm. of mercury, 1 square mm. will sustain $120 \div 16,470 = .0072$ mm., which represents the actual blood-pressure.

In the 128 children examined this formula did not vary more than .0014 mm. Ten showed a blood-pressure per square mm. of .0070 mm. of mercury; ten of .0071 mm.; ten of .0072; eight of .0073; twelve of .0074; fourteen of .0075; twenty of .0076; twelve of .0077; fifteen of .0078; eleven of .0079 and six of .0080 to .0084 mm. The procedure is not so complicated as appears at first glance. Of course, one must always use a cuff of the same width in order to obtain uniform results, and must know what the normal for this width is. Then with a little experience the examiner knows as soon as the arm measurement and height of the

column of mercury are taken, whether the blood-pressure is high or low; or if he is not quite sure, it takes only a minute to make the calculation. He soon learns, also, to know about how many millimeters too high the mercurial column is to give the normal quotient when divided by the circumference of the arm times the width of the cuff; so that he can say such a child has a blood-pressure of 20, 30 or 40 mm. (as the case may be) above or below normal.

Thus we have a standard by which blood-pressure can be expressed, and the measurement of blood-pressure will serve not only as a guide for stimulation, as suggested by Cook and Howland,¹² and for prognosis in the acute infectious diseases, as suggested by Weigert,¹³ but it will also give valuable physical information as to the circulation in all abnormal conditions.

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12. Howland, J.: *Circulatory Failure in the Acute Infections of Children*, Arch. f. Pediat., May, 1910.

13. Weigert, K.: *Ueber das Verhalten des arteriellen Blutdrucks bei den infectiösen Krankheiten*, Samml. Klin. Vortr., 1903, p. 80.

SPONTANEOUS HEMORRHAGE IN THE NEW-BORN *

WITH THE REPORT OF NINE CASES

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I. INTRODUCTION

There are few diseases or conditions in infancy which have attracted more attention than the hemorrhages which occur during the first two weeks of life. The enormous literature devoted to this subject consists in part of case reports and collected statistics bearing on the frequency, the etiology, and the treatment, and in part, of investigations concerning the exact causation of the bleeding.

The anatomic lesions disclosed by post-mortem examination have been inconstant, and divergent views have been held by different observers concerning the causation of the hemorrhage. The so-called hemorrhagic disease of the new-born has been attributed to general diseases, inherited or acquired; to birth injuries; to mechanical causes; and to primary defects or alterations of the blood or vessels.

Within the last few years there have been a number of important investigations on the physiology of the blood, and on the etiology and treatment of various hemorrhagic conditions. It seems that a revision of our ideas concerning the whole group of hemorrhagic diseases is at hand.

A review of the literature, and a study of nine cases of spontaneous hemorrhage in new-born infants, serve as the basis of this communication.

II. CLASSIFICATION

The hemorrhages which occur during the first few days of life may be traumatic, accidental, or spontaneous. The traumatic hemorrhages are usually due to injuries received during labor or consequent on some operative procedure.

The term accidental may be applied to two varieties of hemorrhage: first, the hemorrhage which may be due to inadequate ligation of the umbilical cord; and second, the slight vaginal bleeding which gives rise to no apparent symptoms and is unaccompanied by bleeding from other sources.¹ The latter is termed physiologic by Lequeux.²

1. According to Eröss (Casuistischer Beitrag zur Pathologie der genitalen Blutungen neugeborenen Mädchen, Arch. f. Kinderh., 1891, xiii, 172), vaginal bleeding in the new-born may occur in association with multiple hemorrhages due to lues, sepsis, etc., but in most instances the vaginal hemorrhage is of no patho-

Judging from published reports, spontaneous hemorrhage may arise from almost any organ or tissue and may be associated with different pathologic conditions. In general, two different classifications have been followed. In some instances the classification is based on the apparent origin of the hemorrhage; in others, an etiologic classification has been attempted.

The whole group of hemorrhages has been included under the *hemorrhagic diathesis* or *disease of the new-born*, or *hemophilia neonatorum*.

According to the origin of the hemorrhage, cases are described as melena, purpura,³ cerebral, umbilical, hepatic or adrenal hemorrhage. In many cases the greater part of the external hemorrhage is from the umbilical cord or from the gastro-enteric tract and the terms melena and omphalorrhagia have been used in a generic sense.

The cases of melena are subdivided into: melena symptomatica, when the hemorrhage is the symptom of some obvious disease; melena spuria, when the blood vomited or in the stools is from sources other than the gastro-enteric tract; and melena vera or idiopathica, when there is no apparent cause for the hemorrhage.

Similarly, the term omphalorrhagia idiopathica has been used for umbilical hemorrhage of obscure causation. Runge⁴ divides the umbilical hemorrhages into two groups. In the first group the hemorrhage is from the lumen of the vessels and may occur (a) before, or (b) after, the separation of the cord. The hemorrhage in the second group is parenchymatous and takes place by oozing as though the blood were "squeezed from a sponge."

The terms melena and omphalorrhagia thus applied do not refer merely to the origin of the hemorrhage, but are descriptive of clinical groups of cases. Although in many instances the external hemorrhage is from a single source, post-mortem examination often shows that the hemorrhage was of multiple origin. Moreover, the clinical picture as evi-

logic significance. Jardine (Vaginal Hemorrhage in the New-born, Brit. Med. Jour., 1897, ii, 652), and many others have reported cases which show the benign nature of vaginal bleeding in the new-born. This variety of vaginal hemorrhage occurred in thirty-five of 10,000 female infants observed by Shukowsky (Metrorrhagia Neonatorum, Jahrb. f. Kinderh., 1903, lviii, 105). Ribemont (Des hémorrhagies chez le nouveau-né, Paris, 1880), collected nineteen cases of benign vaginal bleeding in the new-born in which the patients were observed from three months to twelve years. In seven instances the hemorrhage recurred at more or less regular intervals; in three cases the hemorrhage reappeared one or more times, but at irregular periods, while in nine cases there was no recurrence of the bleeding.

2. Lequeux: Etiologie et pathogénie des hémorrhagies graves du nouveau-né. Paris Thesis, 1906.

3. Allan: Two Cases of Purpura Hemorrhagica Neonatorum, Glasgow Med. Jour., 1907, lxxviii, 155.

4. Runge: Die Krankheiten der Ersten Lebenstage, Stuttgart, 1885.

denced by the onset, the course, and the severity of the hemorrhage, is frequently the same, no matter whether the bleeding is external, from the umbilical cord, the mucous membranes, the skin, or from the internal organs.

Our present knowledge does not admit of an accurate etiologic classification, but from a purely clinical standpoint the spontaneous hemorrhages are separated into two groups. The first group comprises the cases in which the hemorrhage appears as an incident during the course of some definite disease, the symptoms of which are apparently dependent on a general pathologic process. In a second group of cases the hemorrhage dominates the entire clinical picture; the symptoms, and the fatal outcome, when such occurs, are directly referable to the loss of blood. It is with the latter group of cases that this paper is particularly concerned.

III. SYMPTOMATOLOGY

The hemorrhage usually occurs before the tenth day of life and most commonly on the second or third day. The time of onset depends somewhat on the source of bleeding and also on the associated pathologic condition—when such exists.

Premonitory symptoms are often present. The infant cries more than usual, is restless, and refuses to nurse. In many cases of melena there is evidence of abdominal pain. Fever is often present and vomiting or diarrhea may occur. The temperature is influenced to a considerable degree by the type and severity of the hemorrhage. Although the temperature is often elevated at the onset, it usually falls with the occurrence of severe hemorrhage and becomes subnormal when much blood has been lost. The symptoms may be present from one to twenty-four hours before the appearance of the blood. In many cases, however, premonitory symptoms are absent, or the symptoms are so slight that they do not attract attention at the time.

The course and extent of the bleeding are also variable. The hemorrhage may be slight and continuous, or it may be intermittent. In many cases the external hemorrhage is of multiple origin and is very often associated with internal hemorrhage of varying severity. As shown by Lequeux² and others, there may be extensive internal hemorrhage while the external hemorrhage is slight or even absent (Cases 8 and 9, Young and Richards⁵). In some cases the hemorrhage is of sudden onset and causes almost immediate death. This type is most common in the massive hemorrhages into the liver, the lungs, or the adrenal glands.

There is no definite clinical type to which the cases conform. When general symptoms or signs are present they are usually due to some gen-

5. Young and Richards: Hemorrhagic Disease of the New-born, *Boston Med. and Surg. Jour.*, 1910, clxii, 47.

eral disease, of which the hemorrhage is one of the manifestations. The only feature common to all cases is the loss of blood and the resulting anemia.

IV. FREQUENCY

The frequency with which spontaneous hemorrhage occurs in the newborn, varies in the experience of different observers. According to Silvermann⁶ there were thirty-seven cases of gastro-enteric hemorrhage in a total of 29,333 births, and according to Kling⁸ seventeen cases occurred in between 12,000 and 13,000 births. Herrgott⁷ observed two cases in 3,000 births, Holtzschmidt⁹ had fourteen cases from 14,203 births and Shukowsky¹⁰ observed twenty-nine cases in 30,000 births.

According to Winkel,¹¹ Gerhardt¹² and Ribemont,¹³ umbilical hemorrhage occurs once for each 5,000 births. Nohl¹⁴ cites a ratio of one case to 1,816 births and Orlowsky¹⁵ one case to 116 births.

V. ETIOLOGY

During the earlier periods of investigation the so-called hemorrhagic disease was ascribed to widely varying causes. Among these are asphyxia from prolonged labor, general plethora, congestion of the mesenteric arteries, respiratory embarrassment, vascular thrombosis, rupture of blood-vessels, irritation due to swallowed amniotic fluid, and too early ligation of the umbilical cord. Later, the occurrence of melena was explained by some observers on the basis of inflammation of the gastro-enteric tract; by others, the bleeding was thought to originate from ulcers or erosions of the mucous membrane.

In 1871, Grandidier¹⁶ considered that a persistence of the ductus arteriosus and the foramen ovale were factors in the occurrence of umbilical hemorrhage.

Hemophilia. By many of the earlier writers hemophilia was considered an important cause of severe spontaneous hemorrhage in the newborn. *Hemophilia neonatorum* is often used as a generic term for the

6. Silvermann: Quoted by Shukowsky (see Note 10).

7. Herrgott: Quoted by Shukowsky (see note 10).

8. Kling, Lorenz: Ueber Melaena neonatorum; Inaug. Dissert., München, 1875.

9. Holtzschmidt: Melena Neonatorum, München. med. Wehnschr., 1902, xlix, 13.

10. Shukowsky: Melena neonatorum; Magendarmblutungen bei Neugeborenen, Arch. f. Kinderh., 1907, xlv, 321.

11. Winkel: Quoted by Lequeux (see note 2) and by Nohl (see note 14).

12. Gerhardt: Quoted by Lequeux (see note 2) and by Shukowsky (see note 10).

13. Ribemont: Quoted by Lequeux (see note 2) and by Shukowsky (see note 10).

14. Nohl: Gelatinbehandlung der Melaena neonatorum vera und der Omphalorrhagia idiopathica; Inaugural Dissertation, Berlin, 1910.

15. Orlowsky: Quoted by Lequeux (see note 2) and by Shukowsky (see note 10).

16. Grandidier: Die Freiwilligen Nabelblutung in der Neugeborenen, Cassel, 1871.

whole group of spontaneous hemorrhages. As a generic term it is inaccurate and adds confusion, for the greater number of these hemorrhages have no relation to true hemophilia. In most instances hemophilia is not manifested in the new-born. A few cases have been reported, however, which indicate that true hemophilia is sometimes the cause of severe hemorrhage during the first two weeks of life.

There was a family history of hemophilia in fourteen (6 per cent.) of the cases of spontaneous hemorrhage collected by Grandidier in 1871. Wittner¹⁷ observed severe hemorrhage after circumcision in an infant with a definite family history of bleeding. Two brothers and eight uncles had died from hemorrhage following the same operation. Larrabee¹⁸ has collected thirty-seven cases in which hemophilia was the apparent cause of hemorrhage in the new-born. Cases were accepted as hemophilia "(a) if there was a distinct history of this disease in the family, or (b) if the baby recovered from the first hemorrhage, but in after life remained a bleeder." The term hemophilia neonatorum should be restricted to this small group of cases.¹⁹

Bacterial Infection. It has long been recognized that many infectious diseases may present hemorrhagic types and there is considerable evidence to show that bacterial infection may be responsible for hemorrhage in the new-born. This evidence is of both clinical and bacteriologic nature. It was observed by Scanzoni²⁰ and others that hemorrhage was more common in infants during the prevalence of puerperal infection. According to Nicholson,²¹ out of 1,500 births at Sloan Maternity Hospital during a period free from puerperal infection, there were no cases of hemorrhage, but in a subsequent 225 deliveries during the prevalence of puerperal

17. Wittner: Ein Fall von Hämophilie bei einem Neugeborenen, Abstr. Jahrb. f. Kinderh., 1899, i, 178.

18. Larrabee: Hemophilia in the Newly-Born with Report of a Case, Am. Jour. Med. Sc., 1906, cxxxi, 497.

19. There is a variety of severe hemorrhage in the new-born which is perhaps closely related to hemophilia. In the reported cases there was no family history of bleeding, but uncontrollable hemorrhage followed slight surgical operations, such as retraction of the prepuce, circumcision, and cutting the frenum linguae. Cases of this sort have been observed by Ziegel (A Case of Hemophilia Neonatorum, Arch. Pediat., 1908, xxv, 120), Brittin (A Case of Hemophilia Neonatorum, Lancet, London, 1908, ii, 158), and others. Ribemont (See note 1) cites a number of cases in which severe hemorrhage followed slight surgical operations. The possibility of an acquired tendency to bleeding which persists, and is therefore closely related to true hemophilia, cannot be denied, for such cases have been observed by Horder, White (Cases of Acquired Hemophilia, Lancet, London, 1909, ii, 1611), and others.

20. Scanzoni: Quoted by Lequeux (see note 2).

21. Nicholson: Report of a Case of Melena Neonatorum Due Apparently to an Infection by the Bacillus pyocyaneus, Am. Jour. Med. Sc., 1900, cxx, 417.

infection, there were eight cases of hemorrhage. Townsend²² and Ritter²³ observed that hemorrhage occurs with much greater frequency in infants born in maternity hospitals than in private practice. Townsend's statistics show that hemorrhage occurred in 0.67 per cent. of the infants delivered in hospital, while in the out-patient department the incidence of hemorrhage was only 0.1 per cent.

There have been a number of epidemics among the infants in maternity hospitals during which hemorrhage was a frequent symptom. Lequeux² describes an epidemic of streptococcic septicemia during which fourteen infants died within a period of twenty-four days. In six of the cases there were definite hemorrhages.

In the epidemic observed by Kilham and Mercealis²⁴ at the New York Infirmary for Women and Children in 1897, hemorrhage occurred in 18 per cent. of the infants born from February 19 to May 1. At the time there were no cases of puerperal infection in the ward; the cases of hemorrhage occurred in rapid succession, and ceased after the enforcement of proper isolation.

Klebs,²⁵ Ritter,²³ and Ebstein²⁶ observed cases of multiple hemorrhage in the new-born which followed suppuration of the umbilical cord. There was evidence of septicemia in twenty-one of the fifty-one cases of hemorrhage in the new-born observed by Ebstein.

In 1875 Klebs²⁵ described an organism, called by him the *Monas hemorrhagicum*, which he found in the tissues of an infant who had hemorrhage during life. A little later, Eppinger²⁷ discovered what was apparently the same organism in the viscera of an infant who had multiple hemorrhages. Weigert,²⁸ in a case of umbilical infection, found micrococci in hemorrhagic areas in the lungs and kidneys. Rehn,²⁹ in 1878, found micro-organisms in hemorrhagic ulcers of the stomach in a new-born infant. In 1889, Baginski³⁰ isolated *Streptococcus pyogenes* from a case of pyemia with hemorrhagic manifestations.

22. Townsend: The Hemorrhagic Disease of the New-Born, Arch. Pediat., 1894, xi, 559.

23. Ritter: Blutungen im frühesten Kindesalter, Oest. Jahrb. f. Pädiat., 1871, ii, 127; Das Verhältniss der Temporären Hämophilie der Neugeborenen zu Blutungen im Späteren Alter und zu der Blutkrankheit, Prag. med. Wehnschr., 1877, ii, 425 and 445.

24. Kilham and Mercealis: Hemorrhagic Disease of the New-Born, A Report of Ten Cases, Arch. Pediat., 1899, xvi, 161.

25. Klebs: Kenntniss der pathogene Schistomyceten, Arch. f. exper. Path. u. Pharmakol., 1875, iv, 409.

26. Ebstein: Quoted by Runge (see note 4).

27. Eppinger: Beitrag zu den mycotischen Erkrankungen. 1. Hämophilie Neonatorum. Prag. med. Wehnschr., 1877, ii, 794, 814 and 841.

28. Weigert: Quoted by v. Dungern (note 33) and by Finkelstein (note 31).

29. Rehn: Quoted by v. Dungern and by Finkelstein.

30. Baginski: Quoted by v. Dungern (note 33).

Following these observations a number of organisms were isolated in rapid succession from the blood and organs of infants who had hemorrhage during life. The hemorrhages of infectious origin are divided by Finkelstein³¹ into two groups. In the first group are the cases in which the hemorrhage has been ascribed to pyogenic organisms. In some cases there has been definite evidence of pus formation, either in connection with localized suppuration, or as a part of general pyemia. In other cases the pus cocci either alone, or in connection with saprophytic organisms such as the *Bacillus pyocyaneus* or some member of the proteus group, have been held responsible for hemorrhagic forms of septicemia.

In the second group of cases, specific hemorrhage-producing organisms are described as the causative agent. Babes³² described such an organism in 1891 and v. Dungern,³³ Gärtner,³⁴ Lubarsch,³⁵ Babes³² and Finkelstein,³¹ Kilham and Mercealis,²⁴ Mapes,³⁶ and Nicholson,^{21, 37} have isolated organisms of this sort from cases of the so-called hemorrhagic disease. In most instances these organisms produced hemorrhagic inflammation, or hemorrhagic forms of septicemia when injected into rabbits or guinea-pigs.

The results of the bacteriologic studies have been very inconstant; the pus cocci, the colon bacillus, the typhoid bacillus, *Bacillus enteritidis*, *Bacillus lactis aerogenes*, the diphtheria bacillus, the *Bacillus hemorrhagica* of Kolb, the pneumococcus, the pneumobacillus of Friedlander, and several unclassified organisms, have been recovered, either singly or in combination, from the bodies of infants who had hemorrhage during life. It is thus seen that no specific bacterial cause has been discovered. The multiplicity of organisms, and the comparative infrequency with which different observers have isolated the same organism—excepting perhaps the pus cocci—merely indicate that hemorrhage in the new-born may occur during the course of bacterial infection.

There is, in addition, a serious objection to many of the bacteriologic examinations. The evidence in most cases rests on post-mortem examination, which was often made from twelve to twenty-four hours after death. The presence of bacteria in some of these cases may have been due to post-mortem invasion.

31. Finkelstein: Lehrbuch der Säuglingskrankheiten, 1905, first half, 98.

32. Babes: Ueber Bacillen der hämorrhagischen Infektion des Menschen. Centralbl. f. Bakt. u. Parasitenk., 1891, ix, 719.

33. Von Dungern: Ein Fall von hämorrhagische Sepsis beim Neugeborenen, Centralbl. f. Bakt. u. Parasitenk., 1893, xiv, 541.

34. Gärtner: Identischer Bakterienbefund bei zwei Melaenafallen Neugeborener, Arch. f. Gynäk., 1894, xlv, 272.

35. Lubarsch: Quoted by Finkelstein (see note 31).

36. Mapes: Quoted by Holt, The Diseases of Infancy and Childhood, 1903, page 100.

37. Hamill and Nicholson: Infections of the Newborn, Arch. Pediat., 1903, xx, 641.

From a clinical standpoint, most of the cases for which the bacteriologic evidence is strongest belong to the group in which hemorrhage is one of the manifestations of a recognized type of bacterial infection. The presence of some general pathologic process is often shown by fever, of a remittent or intermittent type, jaundice, general symptoms, toxemia and, in some cases, evidence of pus formation. Of the same significance is the post-mortem evidence of bronchopneumonia or general pyemia. The bacteriolytic examination has been positive in comparatively few of the cases in which in the absence of general symptoms, the hemorrhage was of sudden onset during the first three days, and the only important objective sign was the loss of blood and the resulting anemia.

Syphilis. Perhaps of next importance to bacterial infection as a cause of hemorrhage in the new-born, is congenital syphilis. In 1876, Epstein³⁸ referred to congenital lues as a cause of hemorrhage in the new-born, probably induced by changes in the capillary walls. Behrend³⁹ came to the same conclusion and used the term "syphilis hemorrhagica neonatorum" to describe a group of cases in which hemorrhage occurred in connection with well-defined luetic lesions. Shutz⁴⁰ and Esser⁴¹ also considered that the lesions of congenital syphilis were a frequent cause of hemorrhage in the new-born.

The presence of vascular changes was denied by Fischl⁴² who doubted the importance of syphilis as a direct cause of hemorrhage. The views of subsequent writers show considerable divergence, and it is perhaps best to cite some of the evidence on which these views were based. Kassowitz and Hochsinger⁴³ in 1886 found micrococci in the organs of infants with congenital syphilis. Kolisko,⁴⁴ in the same year, and Chotzen⁴⁵ in 1887 confirmed these observations and concluded that the feeble resisting power of the infants constituted a predisposition to bacterial infection. Later, Neumann,⁴⁶ Peterson,⁴⁷ Finkelstein,^{31, 48} and others, recovered

38. Epstein: Quoted by Runge (see note 4).

39. Behrend: Quoted by Finkelstein (note 31) and by Mracek (see note 54).

40. Shutz: Quoted by Finkelstein (note 31) and by Mracek (see note 54).
41. Esser: Enteritis Syphilitica unter dem Bilde der Melaena Neonatorum, Arch. f. Kinderh., 1901, xxxii, 177.

42. Fischl: Zur Kenntniss d. hämorrhagische Diathese hereditär-syphilit. Kinder, Arch. f. Kinderh., 1887, viii, 10.

43. Kassowitz and Hochsinger: Ueber einen Mikroorganismus in den Geweben hereditär-syphilit. Kinder, Wein. med. Blatt., 1886, ix, 1, 34, and 70.

44. Kolisko: Ueber den Kassowitz-Hochsinger'schen Micrococccenbefund bei Lues congenita, Wien. med. Blatt, 1886, ix, 97 and 133.

45. Chotzen: Ueber Streptococccen bei hereditär-syphilit. Vierteljahressch. f. Dermat. u. Syph., 1887, xiv, 109.

46. Neumann: Fall von Melaena Neonatorum mit Beimerkungen über die hämorrhagische Diathese Neugeborener, Arch. f. Kinderh., 1891, xii, 54; 1891, xiii, 211.

47. Peterson: Quoted by Finkelstein (note 33) and by Mracek (see note 54).
48. Finkelstein: Ein Fall von hämorrhagische Diathese, Berl. klin. Wehnsehr., 1895, xxxii, 497.

bacteria from the blood and organs of congenital syphilitic infants who had hemorrhage during life. They concluded that hemorrhage due to congenital syphilis alone does not occur. Simon,⁴⁹ Henoeh,⁵⁰ Hamill and Nicholson,³⁷ and others held the same view and considered that congenital syphilis was merely a predisposing factor to bacterial infection — the direct cause of the hemorrhage.

On the other hand, Wilson⁵¹ believes that congenital syphilis is an important cause of the so-called hemorrhagic disease. There was a definite history of syphilis in one of the parents, or evidence of the disease in the infant, in ten out of forty-five cases of hemorrhage cited by Wilson. Hess⁵² and Escalon⁵³ also believe that in some cases congenital syphilis may be the sole cause of hemorrhage.

The main objections which have been raised to congenital syphilis as the direct cause of hemorrhage in the new-born are as follows: (1) that some observers were unable to demonstrate vascular changes in syphilitic infants; (2) that congenital syphilitic infants are predisposed to bacterial infection; (3) that bacteria have been found in some cases of hemorrhage in infants suffering from congenital syphilis.

There are, however, a number of observations which indicate that these objections are not applicable to all cases. In 132 autopsies on congenital syphilitic infants studied by Mracék,⁵⁴ hemorrhage of some grade was found in forty-four, or one-third of the cases. The cases were divided into two groups. In one group there were twenty-three cases in which the hemorrhage was confined to a small part of the body or to a single organ. This group was termed "hemorrhage in syphilitic infants." The second group comprised nineteen cases of multiple hemorrhage to which the term "syphilis hemorrhagica neonatorum" was applied. In these nineteen cases, ten of the mothers had well-defined secondary lesions at the time of confinement. The remaining nine had syphilis shortly before confinement and showed residua in the form of scars, pigmentation, and glandular enlargement. To none of the mothers had thorough treatment been given. The liver, lungs and epiphyses of the infants showed the characteristic syphilitic lesions. Mracék was able to demonstrate changes in the smaller veins and capillaries and the bacteriologic examination made in four cases by Paltauf and Kolisko was negative.

49. Simon: Quoted by Finkelstein (see note 33).

50. Henoeh: Vorlesungen über Kinderkrankheiten, Berlin, 1893.

51. Wilson: Hemorrhage of Syphilitic Origin in the New-born, Arch. Pediat., 1905, xxii, 43.

52. Hess: Syphilis Hemorrhagica Neonatorum, Arch. Pediat., 1904, xxi, 598.

53. Escalon: Des Hémorrhagies gastrointestinales des nouveau-nés. Abstr. Centralbl. f. Gynäk., 1908, xxxii, 1679.

54. Mracék: Syphilis Hämorrhagica Neonatorum, Vierteljahressch. f. Dermat. u. Syph., 1887, xiv, 117.

Cases have been collected by Lequeux² and others in which hemorrhage occurred in luetic infants in the presence of a negative bacteriologic examination. Swartz and Ottenberg⁵⁵ have recently reported a case of multiple hemorrhage in a luetic infant in which an *intra vitam* blood-culture was negative. The liver and spleen were enlarged, spirochetes were demonstrated in the former, and a positive Wassermann reaction was obtained in the cerebrospinal fluid.

In most of the reported cases the diagnosis of syphilis was based on the family history, or on the anatomic evidence of the disease. We have observed two cases of hemorrhage in the new-born in which a positive Wassermann reaction suggested syphilis as an etiologic factor. Both cases terminated in recovery and neither showed any clinical sign of the disease. In one case (Case 3) the syphilitic origin of the hemorrhage is supported by the apparent influence of mercurial therapy; in the other (Case 1) by a negative blood-culture.

Judging from the evidence which has been quoted, it seems that most writers agree that congenital syphilis is a predisposing cause of hemorrhage. Whether the lesions of syphilis may be the sole cause, is a disputed question, but the available evidence indicates that in some cases, at least, congenital syphilis is the only determinable factor.

Cerebral Injury. The view that cerebral injury is an important cause of melena in the new-born is advocated by Pomorski⁵⁶ and v. Preuschen.⁵⁷ Pomorski extended the observations of Brown-Séquard, Schiff, Ebstein and Klosterhalfen and found that various brain injuries in dogs gave rise to hyperemia and hemorrhage in the lungs and to hyperemia, hemorrhage and ulceration in the stomach. Von Preuschen found cerebral hemorrhage in two cases of melena and in collected statistics he noted that of forty-six cases of melena the labor had been difficult or prolonged in thirty-two. He also found that cerebral hemorrhage was present in three of the five cases in which the brain had been examined.

It is difficult to judge the value of this hypothesis. A number of cases have been reported in which hemorrhage was found in various parts of the brain, and in which there was no evidence of gastro-enteric hemorrhage (Couvelaire⁵⁸). Cases of melena have also been observed in which there was no evidence of brain injury. It therefore seems improbable that cerebral injury is a constant, or even frequent, cause of gastro-

55. Schwarz and Ottenberg: The Hemorrhagic Disease of the New-Born, with Special Reference to Blood Coagulation and Serum Treatment, *Am. Jour. Med. Sc.*, 1910, cxi, 17.

56. Pomorski: Experimentelles zur Aetiologie der Melaena neonatorum, *Arch. f. Kinderh.*, 1892, xiv, 165.

57. von Preuschen: Melaena neonatorum. *Centralbl. f. Gynäk.*, 1894, xviii, 201.

58. Couvelaire: Hémorrhagies du système nerveux cérébral des nouveau-nés, *Ann. de gynec. et d'obst.*, 1903, lix, 253.

enteric hemorrhage in the new-born, but it is possible that some cases are of such origin.

Local Causes. In addition to the general causes which have been considered, there are certain local causes which have been considered responsible for hemorrhage during the first week of life. The most common is ulceration in some part of the gastro-enteric tract. Billard⁵⁹ in 1828 referred to cases in which ulceration of the stomach or duodenum was found on post-mortem examination, and similar cases have been cited by Landau,⁶⁰ Dusser,⁶¹ Bauer,⁶² Goodheart,⁶³ Grainger-Bisset,⁶⁴ Chrzanowski,⁶⁵ Silbermann,⁶⁶ Spiegelberg,⁶⁷ Rheiner,⁶⁸ Hecker⁶⁹ and many others. The ulcers are most common in the stomach or duodenum, but sometimes occur in the lower part of the esophagus. In some instances the ulcers are of considerable size and present the same general appearance as those found in adults. Fenwick⁷⁰ in 1900 was able to collect reports of eighteen cases of definite gastric ulcer in infants and young children. Bauer described a case of gastro-enteric hemorrhage in a new-born infant apparently due to a punched out gastric ulcer 4 by 3.4 mm. in diameter. Goodheart described a somewhat similar case in which the eroded vessel could be seen in the base of the ulcer. Landau cites a case of duodenal ulcer with fatal hemorrhage due to erosion of a branch of the gastroduodenal artery. The ulcer measured 8 by 6 mm. In Hecker's case two ulcers were found, one of which had a diameter of 1.5 cm. In many of the reported cases the ulcers were very small and in some instances were only of microscopic size. In other cases hemorrhagic erosions were present.

In cases of melena the gastro-intestinal mucous membrane may be intensely congested, and Shukowsky¹⁰ believes that gastro-enteric hemorrhage is often due to hemorrhagic gastro-enteritis or ileocolitis.

Blood or Vascular Changes or Defects. In addition to the etiologic factors which have been considered, the ultimate cause of the uncontrol-

59. Billard: *Traité des maladies des enfants nouveau-nés*, etc., Paris, 1828.

60. Landau: *Ueber Melaena des Neugeborenen*, etc., Breslau, 1874.

61. Dusser: Quoted by Pomorski (note 56) and by Finkelstein (see note 33).

62. Bauer: *Zur Aetiologie der Melaena neonatorum*, *Centralbl. f. Gynäk.*, 1905, xxix, 1169; *Münch. med. Wehnschr.*, 1904, li, 1207.

63. Goodheart: *Tr. Lond. Path. Soc.*, 1881, xxxii, 86.

64. Grainger-Bisset: *A Case of Perforated Gastric Ulcer with Fatal Hemorrhage from the Bowel in an Infant Forty-five Hours Old*, *Lancet*, London, 1905, ii, 78.

65. Chrzanowski: *Zwei Fälle von Malaena neonatorum*, *Abs. Jahrb. f. Kinderh.*, 1899, i, 176.

66. Silbermann: *Ueber Melaena vera neonatorum*, *Jahrb. f. Kinderh.*, 1877, xi, 378.

67. Spiegelberg: *Ein Fall von Melaena neonatorum*, etc., *Abs. Jahrb. f. Kinderh.*, 1899, i, 176.

68. Rheiner: *Ueber Melaena neonatorum*, *Abs. Jahrb. f. Kinderh.*, 1899, i, 176.

69. Hecker: Quoted by Ribemont (see note 1).

70. Fenwick: *Ulcer of Stomach and Duodenum and its Consequences*, London, 1900.

lable hemorrhage is to be sought in some abnormal condition of the blood. It is a common observation in cases of hemorrhage in the new-born, that the blood may remain fluid many hours after death. In 1850, Bowditch⁷¹ noted the lack of blood coagulation in a fatal case of umbilical hemorrhage. Weber,⁷² in 1851, referred to the futility of local measures to control the hemorrhage and noted that there was a great delay, if not an entire absence, of coagulation in the flowing blood. In 1852, Minot⁷³ in describing the hemorrhagic diathesis of the new-born referred to "the thin watery condition of the blood, and its great deficiency in fibrin, whereby mechanical means become almost wholly inefficacious to arrest its flow." Wilson, Lucas,⁷⁴ and many other writers, have suggested that the continued hemorrhage was dependent on delayed or incomplete coagulation of the blood.

TABLE SHOWING TIME OF COAGULATION OF BLOOD DURING HEMORRHAGE AND AFTER RECOVERY IN SEVEN CASES

Case	Coagulation Time During Hemorrhage, Minutes	Coagulation Time After Recovery, Minutes
1.	No trace of coagulation at the end of 1½ hours.	4*
2.	Few fibrin flocculi at the end of ½ hour. No definite clot...	3 to 4*
3.	9†	8½†
4.	5¾†	7†
5.	9†	3¾†
6.	3½†	
7.	6†	1½†

* Determined by Hinman and Sladen's modification of the method of Milian. In six normal new-born infants, the coagulation time with this method varied from four to five minutes (room temperature).

† By a slight modification of the method of Vierordt. Dr. H. Lett has found that with this method the normal coagulation time in the new-born is 2.3 to 3 minutes at a temperature of 35 to 40 C. (Personal communication.)

In one case observed by Finkelstein,³¹ only slight signs of coagulation were noted after twelve hours; in a second case there was no trace of coagulation at the end of forty-eight hours. According to Finkelstein the main characteristics of the hemorrhagic diathesis of the new-born are the uncontrollable nature of the hemorrhage, and a loss or delay of blood coagulation. Luqueux² states that in these cases the clotting of the blood

71. Bowditch: On Hemorrhage from the Umbilicus in New-Born Children; with Cases. *Am. Jour. Med. Sc.*, 1850, xix, 63.

72. Weber: Beiträge zur pathologischen Anatomie der Neugeborenen, Kiel, 1851.

73. Minot: On Hemorrhage from the Umbilicus in New-Born Infants; with an Analysis of Forty-Six Cases, *Am. Jour. Med. Sc.*, 1852, xxiv, 310.

74. Lucas: Recent Experimental Work on Hemorrhagic Conditions, *Boston Med. and Surg. Jour.*, 1909, clxi, 731.

is retarded, and the retraction of the clot, though not absent, is slow and often incomplete.

Schwarz and Ottenberg⁵⁵ have recently called attention to impaired blood coagulation as the immediate cause of uncontrollable hemorrhage in the new-born. From their experiments they considered that the impaired coagulability is probably due to a destruction of, or to interference with, the production of thrombokinase.

The coagulation time of the blood was determined in seven of our cases. The data are shown in the accompanying table.

The above results do not show a constant delay of blood coagulation. In cases 1 and 2, coagulation was greatly delayed if not entirely absent. In Cases 3 and 5 coagulation was slightly delayed; in Cases 4 and 7 the delay is questionable, while in Case 6 the coagulation time was normal.

This same variation is shown in the observations made after the cessation of the hemorrhage. After recovery, the coagulation time was normal in the two cases (1 and 2) in which it was previously greatly delayed or absent, and in one case (5) in which it had been slightly delayed. In one case (3), however, the coagulation time was practically the same during the bleeding and after its cessation, while in Case 4 the onset of coagulation was later, after the hemorrhage had ceased. In Case 7 the coagulation time was greatly decreased after recovery from the hemorrhage, though it was very slightly, if at all, delayed at the time of actual bleeding.

From these observations it seems that an absence, or a delayed onset of coagulation is not constant in the hemorrhagic conditions of the new-born. Lequeux observed a case of multiple hemorrhage in a new-born infant in which the blood coagulated completely in six minutes, the same time as a specimen of normal blood used as a control.

In our cases which showed a normal or only slightly delayed coagulation time, the readings were taken from the first appearance of clotting and no observations were made on the completeness of clot formation or on the clot retraction. It has been observed in other hemorrhagic conditions that the onset of coagulation may be within the normal time but that clot retraction is defective or absent. This condition has been attributed by Duke⁷⁵ and others to a lack of blood-platelets.

Whipple and Hurwitz⁷⁶ observed a marked tendency to continued bleeding in dogs suffering from necrosis of the liver due to chloroform poisoning. They found that there was a deficiency of fibrinogen, and though a loose-meshed clot was formed, it was unable to check even capil-

75. Duke: The Relation of Blood Platelets to Hemorrhagic Disease, *Jour. Am. Med. Assn.*, 1910, lv, 1185.

76. Whipple and Hurwitz: Fibrinogen of the Blood as Influenced by the Liver Necrosis of Chloroform Poisoning, *Jour. Exper. Med.*, 1911, xiii, 136.

lary hemorrhage. The hemorrhagic condition was therefore due to incomplete, rather than a lack of, blood-coagulation.

It is quite possible that incomplete, instead of delayed, coagulation is the underlying cause of the hemorrhage in some cases of continued bleeding in the new-born.

The delayed coagulation in Cases 1 and 2 was shown by the following experiments to be due to a deficiency or absence of thrombin:

Experiment 1.—Coagulation did not occur after the addition of calcium chlorid.

A deficiency of calcium was therefore not the cause of the delayed coagulation.

Experiment 2.—The addition of normal defibrinated human blood caused the infant's blood to coagulate completely in three to four minutes.

This experiment showed that there was no deficiency of fibrinogen, and also that an "antithrombin" was not the cause of the delayed blood coagulation. The defibrinated blood is supposed to contain thrombin and thrombokinase, either (or both) of which was responsible for the coagulation of the infant's blood.

Experiment 3.—Defibrinated human blood which had been heated to 60 to 63 C. for thirty-five minutes to destroy the preformed thrombin caused the infant's blood to clot in six to seven minutes. Coagulation, however, was incomplete and the resulting clot soft and gelatinous.

These results suggest a blood state similar to that found by Sahli⁷⁷ in hemophilia, which results were interpreted to indicate a deficiency of thrombokinase.⁷⁸ The evidence for this view is not conclusive, however, for Howell⁷⁹ has recently obtained a pure thrombin which under certain conditions is not destroyed by heat even greater than that used in the third experiment. It is possible that the preformed thrombin is not destroyed by this amount of heat and that the activity of the defibrinated blood was still due to thrombin and not necessarily to thrombokinase.

In addition to a deficiency of thrombin or its precursors (prothrombin and thrombokinase), defective blood-coagulation may be due to inhibiting substances or "antithrombin," to a deficiency or inavailability of calcium salts, or to a lack of fibrinogen. Any of these factors may therefore be responsible for uncontrollable hemorrhage. The observations on the blood state in the hemorrhagic conditions of the new-born are too meager to show whether the hemorrhage is always dependent on a single factor,

77. Sahli: Ueber das Wesen der Hämophilie, Ztschr. f. klin. Med., 1905, lvi, 264; Weitere Beiträge zur Lehre von der Hämophilie, Deutsch. Arch. f. klin. Med., 1910, xcix, 518.

78. From the results of a different method of investigation, Addis (Hemophilia, Brit. Med. Jour., 1910, ii, 1422) believes that the blood defect in hemophilia lies in the activation of prothrombin rather than in a deficiency of thrombokinase.

79. Howell: The Preparation and Properties of Thrombin, Together with Observations on Antithrombin and Prothrombin. Am. Jour. Physiol., 1910, xxvi, 253.

or whether the blood defect varies in different cases. A consideration of the fact that the coagulation time is normal in some of the cases and greatly delayed in others, and that hemorrhage in the new-born is due apparently to different pathologic conditions, suggests that the cause of the persistent bleeding is not uniform.

It seems highly probable that vascular lesions play an important part in the production of hemorrhage. The exact pathology, however, is not well understood.

The coagulation of the blood is apparently the normal mechanism for the control of hemorrhage, a defect of which would give rise to persistent bleeding. But it is difficult to understand how a reduction of the blood coagulability can be sufficient in itself to inaugurate the bleeding. The immediate cause of the hemorrhage is probably dependent on some vascular lesion; the uncontrollable nature of the bleeding on defective blood-coagulation.

By some writers vascular lesions have been considered a cause of hemorrhage in congenital syphilis. In the presence of defective blood-coagulation, it is probable that uncontrollable hemorrhage may result from slight traumatic lesions which under other circumstances would be of no consequence. Injuries to the vessel wall may be due to infective emboli and to inflammation. It is also possible that toxic agents may produce vascular lesions sufficient to give rise to hemorrhage.*

It has been mentioned that severe spontaneous hemorrhage in the new-born has been attributed to bacterial infection, to inherited syphilis, to cerebral injury and to local causes such as ulceration and acute congestion. It seems that in the new-born infant there is a general predisposition to severe and uncontrollable hemorrhage for which different agencies may serve as the exciting cause.

There is a type, however, of severe spontaneous hemorrhage, of sudden onset, of short clinical course, without signs other than those dependent on the hemorrhage, for which no definite cause has been demonstrated. The question naturally arises whether these cases might not depend entirely on some primary deficiency of the blood or vessels.

In consideration of the immediate curative effect of blood transfusion, Lambert⁸⁰ and Murphy⁸¹ believe that in melena neonatorum there is a

* It has been shown that when the vessel wall is injured, a substance arises which has at least an accelerating action on blood coagulation (the zymoplastic substance or thrombokinase). (Bernheim: *The Relation of the Vessel Wall to Coagulation of the Blood*, Jour. A. M. A., 1910, lv, 283.) It is possible that this substance is of importance in causing thrombosis of the bleeding vessel and that a deficiency, or interference with the action of this substance may be a factor in the causation of persistent hemorrhage.

80. Lambert: *Melena Neonatorum*, With Report of a Case Cured by Transfusion, Med. Rec., 1908, lxxiii, 885.

81. Swain, Murphy and Jackson: *A Case of Hemorrhagic Disease in the New-born with Transfusion from the Father*, Boston Med. and Surg. Jour., 1909, clxi, 407.

primary blood defect. There was no evidence of syphilis in their cases and it was inconceivable that transfusion could have immediately repaired a vascular lesion or overcome bacterial infection.

Baginski⁸² is also of the opinion that there is a type of hemorrhage in the new-born for which there is no adequate explanation, and which is probably dependent on some primary blood defect or change.

It is unquestionable that there is a clinical type of spontaneous hemorrhage in new-born infants for which no definite etiologic agent has been established. From the evidence available at present, it seems only rational to suppose that the persistent hemorrhage is directly dependent on some biochemical blood defect or change. But whether an abnormality of the blood or vessels is the primary etiologic factor, or whether the hemorrhage is always secondary to some infection or disease, can only be determined by future investigation.

VI. MORTALITY

The mortality in the hemorrhagic conditions of the new-born ranges from 35 to 87 per cent. In the collected cases of Townsend²² the mortality was 79 per cent., in those of Silvermann⁶ 56 per cent. In the personal cases of Townsend the mortality was 62 per cent., in those of Lequeux² 87 per cent. Tarnier⁸³ gives the mortality as 50 per cent., and Minot⁷³ as 84 per cent. In cases of gastro-intestinal hemorrhage Shukowsky¹⁰ observed a mortality of 62 per cent., while in the collected statistics of Vasmer⁸⁴ the mortality was 32.8 per cent. In cases of umbilical hemorrhage Fürth⁸⁵ observed a mortality of 100 per cent., Grandidier¹⁶ of 83 per cent., and Hennig⁸⁶ of 68 per cent.

VII. TREATMENT

The futility of most therapeutic measures in the hemorrhagic disease of the new-born is shown by the high mortality. Recently, however, several measures have been advocated which have given more promising results.

The use of calcium salts to control the hemorrhage has been generally disappointing. Isolated cases have been reported by Doran,⁸⁷ Legge⁸⁸ and others, in which recovery has followed the use of calcium, but in the greater number of reported cases this treatment has been without effect.

Judging from the reports of continental writers, the administration of gelatin is of great value. It was first used for hemorrhage in the new-

82. Baginski: *Lehrbuch der Kinderkrankheiten*, Leipsic, 1905.

83. Tarnier: Quoted by Shukowsky (see note 10).

84. Vasmer: *Ueber Melaena neonatorum*, *Arch. f. Gynäk.*, 1909, lxxxix, 275.

85. Fürth: *Die Nabelblutung*, *Arch. f. Kinderh.*, 1884, v, 305.

86. Hennig: *Gerhardt's Handbuch d. Kinderk.*, 1877, ii, 101.

87. Doran: *A Case of Melena, Recovery*, *Abstr. Arch. Pediat.*, 1909, xxvi, 942.

88. Legge: *A Case of Hemophilia Neonatorum*, *Brit. Med. Jour.*, 1908, i, 1173.

born by Guttman⁸⁹ in 1899, and favorable cases have been reported by Holtzschmidt,⁹ Shukowsky,¹⁰ Grüneberg,⁹⁰ Vasmer,⁸⁴ Torday,⁹¹ Engelmann,⁹² Schubert,⁹³ Heyn,⁹⁴ Sorachowitz,⁹⁵ Nohl,¹⁴ DeBra⁹⁶ and many others. In this country Tuley⁹⁷ has observed cases in which gelatin was of value. Before the use of gelatin, Holtzschmidt⁹ observed fourteen cases of hemorrhage in the new-born in which the mortality was 50 per cent. Five later patients to whom gelatin was administered, all recovered. Nohl reports six cases of gastro-enteric hemorrhage in all of which the patients recovered following the use of gelatin. He has collected statistics which show that in 244 cases of melena before the use of gelatin 113 patients died, a mortality of 46.3 per cent. He found thirty-four cases in which gelatin was used, with only two fatalities, giving a mortality of 5.5 per cent. According to Vasmer⁸⁴ the mortality in sixty-nine cases of melena was 32.8 per cent., but the thirty-seven patients treated with gelatin showed a mortality of only 8.8 per cent.

That favorable results are more often published than ones which are unfavorable, is well known, and this fact must be considered in judging the value of any therapeutic measure from collected statistics. The personal cases of Shukowsky¹⁰ indicate that gelatin is not always as successful as the statistics of Nohl, Vasmer, De Bra, and Holtzschmidt would seem to indicate. The eleven cases with favorable termination were divided by Shukowsky into two groups, mild, and severe. In three of the mild cases the patients recovered under the use of iron sesquichlorid, and in two with the use of gelatin. In three of the six severe cases in which recovery occurred, the patients were treated with gelatin given internally and by subcutaneous injection; two were treated by means of gastric and colonic lavage, while one infant received iron sesquichlorid, ergotin, extract of krameria, musk, and cognac. Four of the patients treated with gelatin died. From these results Shukowsky concludes with Fischer that gelatin is of value, but is useless in the cases of luetic origin, or in those with hemorrhagic gastro-enteritis.

89. Guttman: Zur Behandlung der Malaena neonatorum, Therap. Monatsch., 1899, xiii, 552.

90. Grüneberg: Zur Behandlung der hämorrhagischen Diathese beim Neugeborenen, München. Med. Wehnschr., 1908, lvi, 1, 1079.

91. Torday: Abstr. Jahrb. f. Kinderh., 1903, lvii, 104.

92. Engelmann: Abstr. Jahrb. f. Kinderh., 1910, xv, 433.

93. Schubert: Behandlung der Melaena neonatorum mit Gelatineinjectionen, Centralbl. f. Gynäk., 1907, xxxi, 201.

94. Heyn: Quoted by Schubert (see note 93).

95. Sorachowitz: Zur Behandlung der Melaena neonatorum, Abstr. Centralbl. f. Gynäk., 1907, xxxi, 1454.

96. De Bra: Die Melaena neonatorum und ihre erfolgreiche Bekämpfung durch subcutane Gelatineinjection; Inaugural Dissertation, Berlin, 1910.

97. Tuley: Hemorrhagic Disease of the New-Born, Jour. Am. Med. Assn., 1908, li, 2215.

Following the publications of Weil, animal blood sera have been used for the treatment of hemorrhage in the new-born. The published reports, however, are too meager to form any estimate of its value. Leary⁹⁸ has reported cases in which the patients recovered after the use of rabbit's blood-serum, but he has also had unsuccessful cases. Lucas⁷⁴ observed a favorable result with rabbit's serum. Swain, Murphy, and Jackson report a case in which horse and rabbit sera were ineffectual, but in which the patient was cured by transfusion of human blood.

Judging from recent publications, the most promising line of treatment at the present time is by means of human blood or its derivatives. In 1908 Lambert⁸⁰ reported a case of melena neonatorum in which the patient was treated by transfusion of human blood. The infant had hemorrhage into the skin and subcutaneous tissues, and from the nose and gastro-enteric tract. Recovery ensued immediately after transfusion. Similar cases have been reported by Swain, Murphy and Jackson,⁸¹ Mosenthal,⁹⁹ and Newell.¹⁰⁰ In the cases of Schwarz and Ottenberg,⁵⁵ and Lespinasse and Fischer,¹⁰¹ the transfusion was followed by marked improvement, but the hemorrhage later recurred with fatal result.

In 1910 Welch¹⁰² reported twelve cases of hemorrhage in the new-born successfully treated by subcutaneous injection of human blood-serum. A number of the patients suffered from severe hemorrhage and the treatment was followed by immediate improvement. In a personal communication Dr. Welch informed one of us that up to that time he had treated eighteen such patients without a single fatality due to hemorrhage.

We have treated seven new-born patients with hemorrhage by means of subcutaneous injections of human blood. The first patient was treated in April, 1908, with, first, an injection of 20 c.c. of human blood-serum, and later, an injection of whole blood. The whole blood was used instead of the serum for the reason that it was easier to obtain and could be used immediately, the time required for the serum to separate being saved. It seemed an additional advantage to inject, not only the serum, but also the formed elements which have influence on the coagulation of the blood.

In most cases the blood was taken from one of the parents. The required amount was withdrawn from a vein of the forearm by means of

98. Leary: *The Use of Fresh Animal Sera in Hemorrhagic Conditions*, Boston Med. and Surg. Jour., 1908, iii, 73.

99. Mosenthal: *Transfusion as a Cure for Melena Neonatorum*, Jour. Am. Med. Assn., 1910, liv, 1613.

100. Newell: *Boston Med. and Surg. Jour.*, 1910, clxiii, 435.

101. Lespinasse and Fischer: *Hemorrhage of the Newborn; Treatment by Direct Transfusion of Blood; Review of the Literature, Report of a Case*. Surg. Gyn. and Obst., 1911, xii, 40.

102. Welch: *Normal Human Blood Serum as a Curative Agent in Hemophilia Neonatorum*. Am. Jour. Med. Sc., 1910, cxxxix, 800.

an exploratory syringe and injected immediately into the subcutaneous tissue of the infant's back.

Of the seven infants thus treated six recovered and one died. The fatal case was in an infant who had suffered from multiple hemorrhages for eight days and died three and one-half hours after admission to the hospital. The patient was in a moribund condition when admitted and received only a single injection of 10 c.c. of blood. In five of the six cases in which recovery took place, the hemorrhage ceased soon after treatment, and at the same time there was marked improvement in the general condition. In four cases the hemorrhage was quite severe and the patients presented all of the signs of severe anemia due to loss of blood. One case was of moderate severity. In the remaining case a positive Wassermann reaction was obtained; the hemorrhage was only slightly improved after the blood injections, but ceased after the use of mercurial treatment. Whether the blood injections were of value in this case is difficult to determine.

The subcutaneous injection of whole blood is not without hypothetic objection. The formed elements possibly act as foreign material and must be broken up and excreted. From clinical experience with the method we have found this objection of no obvious importance. In every case the blood was entirely absorbed within a few hours and, so far as could be determined, had no bad influence on the patient's general condition.

It is always hazardous to draw conclusions from small series of cases, and this danger is very real in reference to the treatment of the hemorrhagic conditions of the new-born. The hemorrhages are of varying severity and are due to different causes. Probably some of the cases recover spontaneously, and this is indicated by the number of therapeutic measures which have given favorable results in isolated cases. The true value of any therapeutic agent can be judged only by a large series of cases.

It seems, however, that the best results can be expected from the use of human blood or serum. In the four successful cases the curative effect of blood transfusion was immediate, but this method of treatment must have a rather restricted field. The technical difficulties of transfusion in a young infant are formidable and render the method available only in the hands of a very skilful surgeon.

The value of blood-serum is shown by the results obtained by Welch, and its use is free from the hypothetic objection which applies to the use of whole blood. On the other hand, if the immediate cause of the hemorrhage is the absence of any of the elements essential to blood-coagulation, the use of whole blood would appear to be a more rational procedure. Moreover, the technic is simpler; the whole blood can be used immediately, and in our experience has been efficacious and without apparent harm.

REPORT OF CASES¹⁰³

CASE 1.—The family history was unimportant. The patient, a female infant, was born at the Nursery and Child's Hospital April 13, 1908. The labor was normal. The birth-weight was six pounds.

There was nothing abnormal until April 15, on which day the morning temperature (rectal) was 101 F.; the baby was restless, cried considerably, and made no attempt to nurse. The temperature at 6 p. m. was 102 F. At 8 p. m. about 20 c.c. of blood was expelled from the bowels. Shortly after the hemorrhage, 5 gr. calcium lactate was given by subcutaneous injection, and the same quantity given by mouth every hour for three doses. At 11 p. m. there was a second rectal hemorrhage and at 11:30 a third. A small amount of blood was also vomited. At this time the patient was quite pallid, the skin was dry and wrinkled and the cry very feeble. The rectal temperature was 96 F., the pulse was weak and too rapid to be counted accurately. A fourth hemorrhage occurred at 12 p. m.

At 12:15 a. m., April 16, 20 c.c. of blood-serum from the mother was injected into the subcutaneous tissue of the infant's back. Two hours later a small, slightly blood-tinged stool was passed. It was impossible to judge whether this blood represented a fresh hemorrhage or was the remains of the previous ones. An injection of 10 c.c. of the mother's blood was given at this time. April 16,

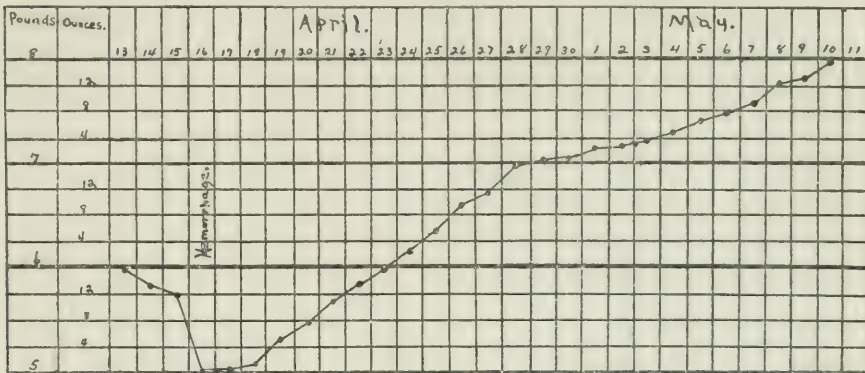


Chart showing weight curve in Case 1, Baby B, breast-fed, having hemorrhages on the fourth day. Treatment by injection of the mother's blood.

the morning temperature was 102 F.; the evening temperature 101. There were no further hemorrhages.

From this time—as shown by the weight chart—the recovery was uneventful. The blood given in the second injection had disappeared entirely by the following morning. April 18, the blood coagulated in four minutes.

Shortly after the first hemorrhage, a deep puncture was made in the lobe of the infant's ear, from which there was a steady oozing of blood. About 1 c.c. of blood was received into a glass tube with drawn out ends and was used to inoculate broth, agar, and blood-serum. The media showed no bacterial growth after incubation at 37 C. for two days.

103. Case 1 was from the service of Dr. C. F. Collins at the Nursery and Child's Hospital. We desire to express our thanks for the privilege of using the history. We are indebted to the late Dr. J. H. McInerney for the opportunity of observing Case 2 and to Dr. Donald MacNaughton for the privilege of reporting Case 9. The remaining cases were from the service of Drs. Judd and Commiskey at the Kings County Hospital in Brooklyn. The blood examinations in these cases were made by Dr. C. Schradeick, resident pathologist at the Kings County Hospital, to whom we wish to express our thanks.

About 1.5 c.c. of blood was collected in a small test tube and at the end of one and one-half hours there was no evidence of coagulation. Two drops of a 1 per cent. solution of calcium chlorid solution, when added to a few drops of the infant's blood, did not cause clotting. The further addition of calcium chlorid was without effect. The remaining blood was divided into two portions, to one of which was added a few drops of defibrinated blood from the mother. A firm clot formed in three to four minutes.

To the second portion of the infant's blood was added a few drops of defibrinated blood which had been heated for thirty-five minutes at from 60 to 63 C. A loose meshed clot was formed in six to seven minutes. The coagulation time of the mother's blood was three and one-half minutes.

This patient was seen October 4, 1910, and at that time weighed thirty-one pounds. There had been no history of bleeding and the blood coagulated in three and one-half minutes. A positive Wassermann reaction was obtained from the blood of both the mother and the child. The mother denied having any manifestation of syphilis. The child had been in good health, with the exception of a persistent nasal discharge at the age of 20 months. The physical examination showed a rather suggestive depression in the bridge of the nose but other stigmata of lues were not observed.

CASE 2.—A male infant, born Jan. 27, 1909, after a normal labor, and weighed eight and one-half pounds at birth. The family history was negative.

Soon after birth a swelling was noted in the occipital region of the skull. The mass was about 5 cm. in diameter; the contents were fluid. On the second day of life the mass had increased to nearly twice its previous size. The baby nursed well, was without fever, and when seen in the forenoon showed nothing abnormal except the hematoma.

January 30, at 6 p. m., a moderate amount of blood was expelled from the rectum and a second smaller hemorrhage occurred during the night. In the forenoon of the next day, January 31, the infant passed two bloody stools and vomited a small amount of blood-stained material. The temperature at this time was 98 F. (rectal) and all feedings were refused. The hematoma seemed about the same size as on the previous day.

At 3 p. m. January 31, 20 c.c. of the father's blood was injected into the infant's back. One-half hour later the baby vomited a small amount of blood-streaked material. A second injection of 10 c.c. of blood was given at 7 p. m. There was no further bleeding. The feedings were taken well and at the end of two weeks the baby appeared to be normal for its age.

January 31, about 1 c.c. of blood was obtained from the baby by means of a lancet-puncture in the heel. After standing for one-half hour the blood showed a few fibrin flocculi but no definite clot was formed. The experiments described under Case 1 were made, with the same results.

After recovery the infant's blood coagulated in from three to four minutes.

CASE 3.—The patient, a male infant, was born at the Kings County Hospital, Dec. 3, 1909. The family history was irrelevant. The head had been born in an occipitoposterior position; at birth the face was edematous, and on each eyelid near the inner canthus was an excoriated area about 1 cm. in diameter. About twenty-four hours after birth blood began to ooze from these areas. Pressure and the application of adrenalin solution did not control the hemorrhage. Ten c.c. of blood from the mother was injected into the subcutaneous tissue of the infant's back. The hemorrhage continued, with perhaps slightly lessened intensity, but in twenty-four hours had resumed its former severity. A second injection of 10 c.c. of blood was given. Twelve hours later the coagulation-time was nine minutes and the hemorrhage had not ceased. A Wassermann reaction was positive and on this basis injections of mercurial ointment were given.

The bleeding began to decrease, and twenty-four hours later had entirely ceased. The infant was discharged in good condition when 14 days old. There was no fever during the hemorrhage and general signs and symptoms were

absent. Three days after the cessation of hemorrhage the blood coagulated in eight and one-half minutes.

CASE 4.—The family history contained nothing of importance. The patient, a female infant, was born at the Kings County Hospital August 28, 1910.

August 30 there was a rather profuse intestinal hemorrhage. During the next twelve hours blood continued to escape from the rectum at intervals and the infant became pale, the face was drawn, and the pulse rapid and weak. Ten c.c. of blood from the mother was injected in the usual manner. At this time the infant's blood coagulated in five and one-half minutes and there was continuous bleeding from the puncture from which the blood was obtained. The bleeding diminished after the blood-injection and had entirely ceased twelve hours later. There were no further intestinal hemorrhages.

After recovery the blood coagulated in seven minutes and there was no continued bleeding from the wound from which the blood was obtained for clinical examination. During the hemorrhage, the temperature was not above normal, and was subnormal (97 F. per rectum) at the time the blood was injected.

CASE 5.—A male infant, born in the Kings County Hospital August 26, 1910. On the day of birth it was noted that there was swelling of the eyelids and that there was a slight oozing of blood from the conjunctiva. August 28, the infant vomited about $\frac{1}{2}$ ounce of bright red blood. During the course of the next twelve hours blood was vomited on three separate occasions. A puncture wound in the lobe of the right ear from which blood was taken for clinical examination gave rise to continuous bleeding. The infant became pale, was feeble, and showed the effect of the loss of blood. Five c.c. of blood from the mother was given in the usual way. There was no further hematemesis. The bleeding from the conjunctiva lessened, but twelve hours later there was still a slight oozing of blood from this source and from the wound in the ear. At this time 10 c.c. of blood, from a healthy antepartum patient in the seventh month of pregnancy, was given.

The hemorrhage ceased within a short time after the last blood injection and did not recur.

During the hemorrhage (before the first blood injection) the coagulation-time was nine minutes; after recovery it was three and three-fourths minutes. The infant's blood gave a negative Wassermann reaction.

CASE 6.—A female infant, 8 days old, was admitted to the Kings County Hospital Sept. 15, 1910. The family history was unimportant.

Shortly after birth there was oozing of blood from the stump of the umbilical cord. Two days later the baby became jaundiced and a few ecchymoses were noted on the right shoulder, the right hand and on the abdomen in the region of the umbilicus. On the sixth day there was a profuse umbilical hemorrhage. The patient was extremely weak.

Adrenalin, gauze pressure, suture, etc., were ineffective in controlling the hemorrhage. On the seventh day there was another profuse hemorrhage from the cord.

At the time of admission the baby was intensely jaundiced, and ecchymotic spots were on the shoulder, abdomen, and right hand. There was continuous oozing of blood from the abdominal end of the umbilical cord. One and a half hours after admission the coagulation-time of the blood was three and one-half minutes. An injection of 10 c.c. of the mother's blood was given at this time. The rectal temperature at the time of admission was 97 F.

Three and a half hours after admission the infant died. Permission for post-mortem examination was refused.

CASE 7.—A male infant, born at the Kings County Hospital Jan. 17, 1911, at 8:20 p. m.

The family history was unimportant. The labor was uneventful; the baby was apparently normal and weighed seven pounds and one ounce at birth.

January 18, about 6 p. m., blood began to ooze from the conjunctiva and the nasal mucous membrane. A small amount of blood was also vomited. The

hemorrhage was slight and ceased spontaneously. Physical examination at this time was negative.

In the forenoon of January 19 there was a reappearance of the conjunctival hemorrhage and there was profuse bleeding from the umbilical cord at its junction with the abdominal wall. The umbilical hemorrhage was checked by local application of 1-1000 adrenalin solution.

At 6 p. m. there was a slight hemorrhage from the umbilicus, which ceased after the use of adrenalin solution.

A profuse umbilical hemorrhage occurred at 10:30 p. m. After using various local measures with no success the umbilical hemorrhage was finally controlled by the application of continuous ligatures over the whole umbilical stump. The hemorrhage from the conjunctiva reappeared and blood was noted in the stools. At this time the infant was pallid and feeble and showed the effect of the repeated hemorrhages.

January 20, 5 c.c. of blood was withdrawn from the median basilic vein of the mother and injected into the muscles of the infant's back.

There was no further hemorrhage and the infant began to improve. January 24, the infant was in good condition and was discharged from the maternity ward. There was no fever during the illness; the highest temperature was 100 F. (rectal).

Coagulation-time of the blood: January 20, six minutes; January 21, five minutes; January 22, one and one-half minutes.

CASE 8.—A full term male infant, born at the Kings County Hospital on Sept. 12, 1910. The birth-weight was five pounds and twelve ounces and the infant was apparently normal. The family history was unimportant.

During the first seven days the baby gained weight and was apparently healthy. On the eighth day the infant refused to take the breast and was fed from a spoon. On the day following, while being fed, the baby suddenly became extremely cyanotic. The pulse was feeble and too rapid to be counted. Death ensued within fifteen minutes.

On post-mortem examination the heart was found congested and both auricles were filled with dark, fluid blood. The lungs were hyperemic and showed scattered areas of atelectasis. Beneath the capsule of the liver there were three or four ecchymoses 2 to 3 cm. in diameter, and small hemorrhages were present throughout the liver substance. The whole organ was extremely congested.

The kidneys were very hyperemic. The brain, spleen, pancreas, suprarenals and thymus were anemic, but were otherwise normal.

The blood throughout the body was dark and showed no evidence of coagulation.

Sections of the liver were stained by the Levaditi method but no spirochetes could be found.

CASE 9.—A male infant, born at the Samaritan Hospital June 9, 1910. The birth-weight was ten pounds.

Nothing abnormal was noted until the seventh day, at which time the baby nursed poorly and vomited several feedings. The vomiting continued, the stools were green and loose, and the temperature ranged from 99 to 106 F. Physical examination disclosed nothing abnormal. On the twelfth day the urine was slightly blood-stained.

The infant died on the thirteenth day without showing any definite signs beyond those already noted.

At the post-mortem examination the mucous membrane of the intestines was moderately congested. With the exception of the right kidney and suprarenal gland the remaining organs showed nothing of importance.

The right kidney and suprarenal were three times the normal size. The suprarenal was practically converted into a blood-cyst by parenchymatous hemorrhage. The pelvis of the kidney was filled with blood and the parenchyma was greatly distended by multiple hemorrhages.

INFLAMMATORY CHANGES IN THE APPENDIX DURING EARLY INFANCY *

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ST. LOUIS

The following report of an investigation of inflammatory changes in the appendix during early infancy is made from the autopsy findings in 200 consecutive cases at the New York Foundling Hospital, from January to September, 1910. The patients selected were the youngest possible, and comparatively few exceeded three months in age.

Ribbert¹ found that obliterative changes in the appendix, regarded by him as a process of physiologic involution, occurred during the first decade in 4 per cent. of cases. MacCarty,² in an extensive study of the material of the Rochester, Minn., clinic, found that partial obliteration of the lumen of the appendix might be present as early as the fifth year, and complete obliteration was seen as early as the tenth year. He estimates that the average time necessary for complete obliteration of the lumen of the appendix is approximately four years, and believes that pathologic processes must determine these rapid changes.

It has long been known that the frequency of appendicitis, seen clinically, increases from infancy through the years of childhood to puberty. Deaver³ has found that the frequency of appendicitis occurring during the first five years of life is about 8 per cent. A good many cases of appendicitis occurring during infancy are now on record, and these are reported most frequently in infants during the latter months of the first year or during the second year. A few rarer instances of appendicitis are reported as occurring as early as the fifth or sixth week. Gastro-intestinal symptoms of varying severity have frequently preceded these attacks. Deiss,⁴ in 1908, reported a case of appendicitis with peritonitis in a child of two weeks. The lesion was found at autopsy, the child exhibiting clinically acute gastro-intestinal symptoms for eight days preceding its death.

The clinical course in the hospital of these infants dying early of malnutrition offers but little of note. A few had been born in the hospital in the obstetrical service, and then transferred to the children's ward. In great part they had been admitted to the institution several

* From the Department of Pathology of Washington University.

1. Ribbert: *Virchow's Arch. f. path. Anat.*, cxxxii, 66.

2. MacCarty: *Jour. Am. Med. Ass'n.*, iv, 488.

3. Deaver: *Jour. Am. Med. Ass'n.*, iv, 2198.

4. Deiss: *Basle Dissertations*, 1908, p. 63.

days after birth, many coming from the city maternity hospitals. Some had been breast-fed, but the majority had been artificially fed from the start. Breast feeding, but more often artificial feeding with some modification of milk, was continued after the child entered the hospital service. On admission these children were in a weak, anemic, often emaciated condition, with all the chief symptoms referable to the gastro-intestinal tract. Temporary improvement was at times seen, but the usual course was a progressive loss of weight, with increasing intestinal disturbance, death occurring quickly in this state of malnutrition.

It is well known that infants dying with severe gastro-intestinal symptoms will often, at autopsy, show only slight anatomic changes. R. Fischl⁵ has recently reviewed these histologic changes of the gastro-intestinal tract in acute and chronic diseases of malnutrition. The stomach is found practically normal. At times the cells in the glands of the stomach undergo a peculiar swelling suggesting a coagulation necrosis. Fischl has found hypertrophic changes in the crypts of Lieberkühn with occasional formation of small cysts. In the more acute cases, the hyperemia of the small intestine in different areas is very marked, and small hemorrhages occur in the mucosa. Near the hemorrhages superficial necrosis of the epithelium is often found. Fischl has pointed out that at times the epithelium appears swollen, with poorly staining nuclei, suggesting an effect which a poison might produce when acting on the cells. The follicles of the large intestine are frequently prominent and surrounded by a zone of hyperemia. In the region of the follicles small ulcers may appear and these are usually of superficial character. Peyer's patches are but little involved. A well-marked hyperemia and a hyperplasia of the mesenteric lymph-nodes has been noted.

A belief that the appendix might offer a point of least resistance to infection of the gastro-intestinal tract, and the hope of finding some etiologic factor explaining the peritoneal exudate found to be present occasionally in such young infants at death, led to a systematic histologic examination of a series of appendices. The material was obtained soon after death, the time varying from a few minutes to twenty-four hours. The appendix and a part of the wall of the cecal region in each case were preserved in formaldehyd solution and the sections cut in paraffin.

Among 200 appendices examined, fifteen showed inflammatory changes of varying intensity. A brief report of these cases follows.

CASE REPORTS

CASE 1.—Autopsy 815. R. D., male aged 1 month, 15 days; length of body 53 cm.

Anatomic Examination.—On opening the abdomen the intestines are found considerably distended, injected and matted together by thick yellowish pus. The

5. Fischl, R.: In Pfaundler and Schlossman, *Disease of Children*, iii.

greatest collections of purulent matter seems to be in the lower abdomen. In places the adhesions are very dense, especially in the region of the cecum, and when this is lifted from the posterior parietes, a small abscess containing thick green pus is entered. The greater part of the appendix has been destroyed. A small ragged portion of the base measuring about .5 cm. arises from the posterior surface of the cecum. A small piece of necrotic tissue (later identified microscopically as appendix tissue) lies in the upper part of abscess cavity, hanging loosely to the posterior surface of the colon. The mucosa of the large intestine is intensely congested; it contains many small superficial ulcers in the site of the follicles of the cecal region, of the hepatic flexure and of the sigmoid. No ulcer has caused perforation. The small intestine in places is a good deal congested, but has no ulceration. The stomach, liver, spleen, kidneys, lungs and heart seem normal. Smears from the exudate of the peritoneum show the presence of pus and streptococci.

Microscopic Examination.—A section has been taken through the base of the appendix. The mucous membrane is destroyed; there is intense infiltration of muscularis and serosa, with polynuclear leukocytes and lymphocytes. A similar inflammation is found in the portion representing the remains of the tip of the appendix found in the abscess cavity adherent to the colon. Sections through the ulcers of the large intestine show that these are small and superficial. Sections of the other viscera are normal. Liver sections stained for *Spirochæte pallida* are negative.

CASE 2.—Autopsy 812. M. O., female, aged 24 days; length of body 49 cm.; weight 5 pounds. Autopsy confined to abdomen and thorax.

Anatomic Examination.—On opening the abdomen the intestinal coils are slightly distended, considerably injected and loosely glued to one another by a thin, yellowish exudate. This exudate is greatest in amount in the lower abdomen, especially on the right side. The cecum is found in the iliac fossa loosely bound to the abdominal wall by yellow exudate. The appendix, measuring 4.5 cm., hangs over the pelvic brim. It is swollen and dark red; the tip is almost black in color, but shows no perforation. The pelvic organs are all deeply congested, and the right tube is dark red in color. The liver, kidneys and spleen are normal in size and form. The thoracic viscera are apparently normal, save that the lungs are hyperemic, especially at the bases. The large intestine has areas where the mucous membrane shows deep congestion, with marked prominence of the follicles. On gross examination no ulcerations are found. There is deep congestion of the mucosa of the small intestine in places. Smears from the peritoneal exudate show the presence of pus cells and staphylococci.

Microscopic Examination.—The appendix was sectioned in a number of places; the mucosa of the tip is almost entirely destroyed. The muscle-coats and serosa are edematous and intensely infiltrated with polynuclear leukocytes and lymphocytes. Lymph-vessels and veins are distended with leukocytes. There is thrombosis of a medium sized artery in the mesentery close to the outer muscle-coat. The tissue nearest the mesentery is best preserved, while that opposite the mesenteric border is almost entirely necrotic. In sections made near the base, the inflammation is much less marked. The cecum near the origin of the appendix shows the serosa alone involved. Sections made through the uterus and both Fallopian tubes present a normal mucosa and muscularis, but the serosa is very edematous and densely infiltrated with inflammatory cells. The other viscera are practically normal. *Spirochæte pallida* could not be demonstrated in the liver.

CASE 3.—Autopsy 1007. H. J., male, aged 17 days.

Anatomic Examination.—The body is that of a poorly nourished infant 46 cm. in length. The skin is slightly jaundiced having a light yellowish color. Examination is confined to abdomen and chest. On opening the abdomen the intestines appear congested and are bound together loosely by what appears to be a thin

fibrinous exudate, confined mostly to the lower right side. The cecum is found in the iliac fossa fixed well forward, close to the anterior abdominal wall; its presenting lower margin is adherent to the peritoneum covering the iliac fossa by flakes of fibrin. The appendix passes inward and to the left over the psoas down into the pelvis. It is much swollen, deep, dark red, especially near the tip, and is adherent to the brim of the pelvis in its inner third and adherent to the sigmoid in its outer two-thirds, the sigmoid being a large loop extending to the right beyond the mid-line of the body. The mesentery of the appendix shares in these loose adhesions. The adjacent lymph-glands seem moderately swollen and larger than the mesenteric glands elsewhere.

Examination of the appendix shows that it is 5 cm. long. The walls appear thickened and the mucous membrane dark red; the lumen contains a brownish red substance. In the smears taken from the peritoneal cavity are pus cells and Gram-negative bacilli suggesting the colon type. The mucous membrane of the stomach, the lower part of the small intestine and the entire large intestine are distinctly congested. The lymph-follicles of the large intestine are quite prominent and surrounded by a reddened zone; apparently nowhere is there ulceration that can be appreciated on gross examination. The gall-bladder has a normal appearance and is filled with thick, dark bile. The hepatic and common bile ducts are patent.

Microscopic Examination.—The sections are made through the appendix and the sigmoid at the point of maximum adhesion. The sigmoid appears quite normal, save that the serosa is very edematous and shows the presence of many leukocytes and lymphoid cells. In contrast with the appearance of the sigmoid, the wall of the appendix is uniformly, in some places very densely, infiltrated with inflammatory cells. Sections made from other parts of the intestine and other viscera present nothing unusual, save that the kidneys show a moderate parenchymatous degeneration.

CASE 4.—Autopsy 900. H. H., male, aged 27 days; length of body 51 cm.

Anatomic Examination.—The cecum is in the iliac fossa, and the fixation of the colon occurs below the iliac crest. The appendix measures 3.5 cm. in length, and arises posteriorly. The first part of the appendix lies in an erect position behind the cecum and the ascending colon. As it meets the reflection of the peritoneum from the colon to the iliac fossa, a sharp bend occurs directing the tip of the appendix downward and inward. The entire appendix is fixed to the cecum and the iliac fossa, save a small part of the tip, which remains free. At the bend in the appendix there is a good deal of redness and edema.

Microscopic Examination.—The mucosa and the submucosa opposite the mesenteric border are necrotic, but in other parts are fairly well preserved. There is intense infiltration of the muscularis and the serosa everywhere. There is a thrombosis of one of the larger arteries in the wall of the appendix near the mesentery which has resulted in partial occlusion of the vessel.

CASE 5.—Autopsy 890. E. C., female, aged 24 days; length of body 50 cm.

Anatomic Examination.—The cecum is found in the iliac fossa and the proximal part of the ascending colon is fixed to the iliac fossa at a point below the iliac crest. The appendix, 4 cm. in length, passes up and inward, the distal part lying behind the terminal coil of the ileum. The appendix looks moderately swollen and congested, and is covered in places by a few small flakes of yellowish fibrin.

Microscopic Examination.—The mucosa is well preserved and the lumen contains many pus-cells, a moderate number of red blood-cells and bacteria. The muscularis and serosa are moderately swollen and show the presence of a fair number of leukocytes scattered here and there. The sections through the wall of the cecum are normal.

CASE 6.—Autopsy 1015. V. R., male, aged 24 days; length of body 48 cm.

Anatomic Examination.—The body is that of an emaciated infant 50.5 cm. long; weight about 4 pounds. Examination confined to abdomen and chest. On opening the abdominal cavity, the small intestine is very moderately distended. The cecum is in the iliac fossa; the proximal ascending colon is fixed to the iliac crest by a small mesocolon. The appendix 4 cm. in length, passes upward and to the left so that the tip lies behind the terminal coil of the ileum. It is bent on itself near the middle, and appears red and moderately swollen. On splitting open the appendix the walls seem thickened; the mucous membrane appears dark red in color. The lumen contains a reddish brown fecal matter. The adjacent cecum shows also a congested mucous membrane, but it has not as deep a color as the appendix. The lymph-follicles of the large intestine stand out prominently, but without evidence of ulceration. The small intestine and the stomach are of normal appearance.

Microscopic Examination.—The inflammatory changes in the appendix are of slight character. There is a moderate infiltration with inflammatory cells of the muscular coat and the peritoneum, especially in the region of the mesentery. The cecum is normal.

CASE 7.—Autopsy 912. H. L., female, aged 1 month, 5 days.

Anatomic Examination.—The cecum is in the iliac fossa and the proximal part of the ascending colon is fixed to the posterior parietes, above the level of the iliac crest. The ascending colon has no mesentery. The appendix, measuring 4 cm. in length, extends straight upward behind the first part of the ascending colon, but is not adherent to either. It has no deflections. It appears slightly reddened and swollen.

Microscopic Examination.—The mucosa is well preserved and shows but little change. Submucosa, muscularis, and the serosa are infiltrated with a considerable number of leukocytes, lymphocytes, and eosinophil cells. The section of the cecum presents a small area in the muscularis with a similar infiltration, but this is not very extensive.

CASE 8.—Autopsy 888. V. Y., male, aged 30 days; length of body 49.5 cm.; weight 5 pounds.

Anatomic Examination.—The cecum is found in the iliac fossa; the colon is fixed to the iliac crest without a mesentery. The appendix arises posteriorly and lies directly behind the cecum and the first part of the ascending colon. It measures 4.5 cm. in length and is bent on itself near its mid-point so that the distal part lies parallel to the proximal part. The entire appendix seems swollen and injected and is covered with a fine yellowish exudate. Smears made from the exudate contained pus-cells, degenerated epithelial cells, a few streptococci and many Gram-negative bacilli. Cultures contained *B. pyocyaneus*.

Microscopic Examination.—The mucosa of the appendix is poorly preserved because of autolytic changes. The muscularis and the serosa are infiltrated with many leukocytes and lymphocytes. Sections made through adjacent lymph-glands exhibit the microscopic evidence of acute inflammation.

CASE 9.—Autopsy 841. E. P., female, aged 23 days; length of body 48 cm.

Anatomic Examination.—The cecum lies in the iliac fossa. The appendix arises from the cecum in the usual manner, passing upward behind the terminal part of the ileum. It has a sharp bend downward near its mid-point. It measures 4 cm. and appears swollen; the tip is reddened and adherent to the cecum and iliac fossa by a loose, fine, yellowish exudate.

Microscopic Examination.—The mucosa is fairly well preserved. The muscle-coats are moderately swollen and show a marked infiltration with polynuclear leukocytes, lymphocytes and eosinophils. The serosa, in which the vessels are greatly engorged, has an infiltration similar to that of the muscularis. There is thrombosis of one of the smaller arteries of the mesentery. Sections from the

wall of the cecum are normal, save for considerable swelling of the serosa, and in places moderate infiltration with polynuclear leukocytes and lymphocytes.

CASE 10.—Autopsy 929. M. G., female, aged 1 month, 3 days; length, 50 cm.

Anatomic Examination.—The cecum is found in the iliac fossa; the proximal colon begins to be fixed to the posterior parietes above the iliac crests at the lower pole of the right kidney. The appendix here again arises posteriorly, and passes directly upward to the lower pole of the right kidney where it becomes bent down and inward. The tip alone is adherent, the adhesion being with the posterior parietal peritoneum. The entire appendix, which measures about 5 cm., seems deeply congested, but especially so in the distal portion.

Microscopic Examination.—The lumen of the appendix appears considerably distended. There is great hyperemia of all the blood-vessels. The mucous membrane contains many polynuclear leukocytes, lymphocytes and eosinophils, and besides has small hemorrhages. The muscle coats are rather thin. The serosa is very swollen and edematous. Considerable numbers of leukocytes and eosinophil cells are found everywhere. The cecum is normal.

CASE 11.—Autopsy 1037. J. S., male, aged 29 days; length of body, 51 cm.

Anatomic Examination.—The cecum lies in the iliac fossa. The appendix arises posteriorly; its proximal part ascends in close relation with the cecum and the ascending colon. Where it meets the reflection of the peritoneum from the colon to the iliac fossa, which occurs below the crest, it is bent on itself like a fish-hook. It appears dark red in color and swollen, especially in the distal part.

Microscopic Examination.—The mucosa in the distal portion of the appendix is poorly preserved. The edematous muscularis and serosa contain many leukocytes. Sections from the proximal part of the appendix are practically free from inflammatory changes. The cecum is normal.

CASE 12.—Autopsy 848. D. L., male, aged 28 days; length of body, 51 cm.

Anatomic Examination.—The cecum is found in the iliac fossa. The proximal part of the ascending colon, having no mesentery, is fixed just below the iliac crest. The cecum turns back sharply and gives rise to the appendix, which lies in an erect position directly behind the cecum and the ascending colon, to both of which it is closely adherent. The tip of the appendix is bent sharply downward, the deflection occurring evidently where the appendix meets the line of fixation of the ascending colon to the iliac fossa. The tip of the appendix is slightly swollen, but very much reddened. The appendix measures 4 cm. in length.

Microscopic Examination.—Nearly the entire mucosa and the submucosa appear granular and necrotic. A small wedge-shaped segment survives and is bounded by a necrotic margin on each side. This small area exhibits marked hyperemia, and contains some extravasation of red-blood-cells. The muscular coat and the serosa are intensely infiltrated with inflammatory cells. This section suggests an infarction with a marked secondary inflammation. The cecum is normal.

CASE 13.—Autopsy 937. D. E., female, aged 13 days; length of body 47 cm.; weight $4\frac{1}{4}$ pounds.

Anatomic Examination.—The cecum is in the iliac fossa, well anteriorly, near the abdominal wall. The ascending colon is fixed in the iliac fossa by a short mesentery. The proximal part of the appendix passes over the psoas muscle; the distal portion lies over the brim in the pelvis. There are no adhesions, but a small amount of fibrin covers a slightly swollen and reddened surface. On opening the appendix, the mucous membrane appears of a red color, and the lumen contains a small amount of yellow fecal matter.

Microscopic Examination.—Small areas of hemorrhage are found in the mucosa, which is very hyperemic. The vessels of the mesentery are distended with blood. In one artery are many leukocytes lying in close contact with the intima. The mesentery and the serosa contain a considerable number of leukocytes and

lymphocytes. The muscularis is very thin and shows only a few inflammatory cells. Sections of the cecum are normal.

CASE 14.—Autopsy 953. M. K., aged 27 days; length of body 50 cm.

Anatomic Examination.—The cecum is undescended and lies above the crest of the ilium, fixed there by irregular adhesions to the posterior parietes and to the lower pole of the right kidney. The appendix lies behind the cecum and the ascending colon and is embedded in the adhesions as far as the tip, which still remains free. The tip of the appendix touches the under surface of the liver and is deflected outward at an angle of about sixty degrees. On gross examination no pathologic changes are apparent.

Microscopic Examination.—A small thrombus in an artery with partial occlusion of the lumen occurs in the outer part of the muscularis. Inflammatory cells in considerable numbers are scattered here and there throughout the section. Sections of the cecum are normal.

CASE 15.—Autopsy 989. M. B., aged 1 month and 22 days; length of body 52 cm.

Anatomic Examination.—The cecum is undescended and lies above the iliac crest below the liver. The appendix hangs vertically downward and measures 4 cm. The mesentery of the appendix is formed by the anterior vascular fold instead of the posterior. The tip of the appendix is congested, but the base has a normal color.

Microscopic Examination.—The tip of the appendix has a good deal of infiltration of its wall with polynuclear leukocytes and lymphocytes. In contrast with this, the sections made through the base exhibit merely mild inflammatory changes.

In the cases above reported, inflammatory changes occurred in the male seven times, in the female eight times. The two youngest infants were 13 days and 17 days old, respectively. In nine instances, the age ranged between 20 and 30 days. Four cases were between a month and two months old.

A reference is made in each protocol to the anatomic relations of the cecum and the appendix. In two instances (Cases 14 and 15) the cecum was still in an incompletely descended position, lying between the iliac crest and the liver; but in the remainder of the cases the cecum occupied its usual position in the iliac fossa. Three times the distal part of the appendix was found hanging over the pelvic brim, and in such instances the distal part gave the evidence of severe inflammation. In eight cases the appendix occupied a position directly behind the cecum and proximal part of the ascending colon. It is in this position of the appendix that in infants sharp angulation frequently occurs. The cause apparently is found in the relatively small retrocolic compartment at the time of birth, to which a relatively large appendix accommodates itself. Thus, the appendix passing upward directly behind the cecum and colon, may be bent sharply downward by the upper limit of the retrocolic space formed by the reflection of the peritoneum from the ascending colon to the iliac fossa or posterior parietes. Under normal conditions, even, fusion of the appendix with the cecum, ascending colon, posterior parietal peritoneum or iliac fossa is frequently found. There may result from these condi-

tions not only a permanent fixation of the sharply bent appendix, but also changes in the form of the mesentery of the appendix, possibly causing circulatory disturbances. In the majority of the cases reported above, inflammation occurred when the appendix was found sharply bent on itself, lying in close relation with the cecum and colon; and in several instances the inflammation was more marked at the site of angulation than in other parts of the appendix. In three cases, the proximal part of the appendix passed upward, inward and to the left, so that the distal part lay curled behind the mesentery of the terminal coil of the ileum. The last described position of the appendix is that most frequently found in infants, as it formed 50 per cent. of all cases in 1,050 autopsies in infants studied by me. It is of interest to note that although the majority of inflammatory changes were found in appendices lying erect directly behind the cecum and colon, this variation in position of the appendix in the infant was found in only about 25 per cent. of all infants. Sharp angulation of the appendix leading to obstruction of the lumen, causing retention of contents in the distal portion of the appendix, may be regarded as a factor influencing the inflammatory changes. Heile⁶ has studied the very rapid destruction of the epithelium and other elements of the intestinal wall experimentally, and believes that these changes are due to bacterial toxins and other chemical poisons elaborated in the decomposition of fecal matter which takes place when obstruction of the lumen has been produced.

The peritoneal exudate found in seven of the cases varied considerably in amount and character. With slight inflammatory changes in the appendix, a light yellowish exudate covered the reddened surface of the appendix and glued it to the adjacent peritoneum. In the severer cases, the picture did not differ from that seen in the adult when a spreading peritonitis occurs. The smears and cultures made from the exudate showed in one case staphylococci, in a second streptococci, and in a third there were bacilli of the colon type. In one instance, the cultures were rapidly overgrown with *Bacillus pyocyaneus*. I have found a similar peritoneal exudate five times in 800 previous autopsies in infants. No histologic examination had been made of the appendix in these instances.

The gross appearance of the appendix in all cases save one, gave evidence of considerable swelling, and of redness that varied from a pinkish color in mild cases occurring merely at the point of maximum inflammation, to the dark reddish brown color seen in the severer forms of inflammation associated with the peritonitis. The mucous membrane in mild cases looked hyperemic, and occasional small reddish petechial spots were found. In severe instances the inner surface appeared dark red and the lumen was filled with a reddish-brown necrotic material. Fecal material was found not infrequently in these appendices, but apparently

6. Heile: Mit. a. d. Grenzgeb. d. Med. u. Chir., xxii, Part 1.

not in the firm masses so commonly seen as enteroliths in inflamed appendices in older children and in the adult. No parasites were found in the lumen on gross or microscopic inspection of the contents of the appendix.

The histologic changes have considerable interest and are of as advanced nature as those often seen in adult inflammatory conditions, when the process is of an acute suppurative character. Aschoff⁷ a short time ago, and Obendorfer⁸ still more recently, have reviewed the histology of the appendix in the new-born and in infancy. Aschoff finds that the lymphatic tissue in the mucosa and in the submucosa is relatively poorly developed at the time of birth. A rapid increase in the lymphatic elements occurs soon after birth and continues steadily until the latter years of childhood, when a decrease of lymphatic tissue gradually takes place. He shows that lymphocytes, "larger lymphoblastic" cells, mast cells and eosinophils are present at the time of birth, but that plasma cells make their appearance only after birth. The surface epithelium at first consists almost entirely of goblet cells, but these decrease in number very soon after birth. The muscle coats in the appendix of the new-born are thin and at times show some irregularities in the density of the muscle bundles. With the general increase of the lymphatic tissue in the mucosa and in the submucosa, groups of lymphocytes are frequently found here and there in the muscularis and serosa and produce an appearance which may simulate inflammation. Aschoff finally points out that the folds in the mucous membrane in the infant's appendix are not as distinct as in later life; the presence of the folds, he thinks, is of importance in the genesis of inflammation.

The earliest changes with inflammation of the appendix are difficult to recognize even in the adult, and could not always be satisfactorily studied in this series of autopsies. Autolytic changes were so rapid in onset, that even in several cases in which the autopsy was done immediately after death, with the body warm, autolysis had begun in the appendix, although the mucosa was well preserved in other parts of the intestine. Even in cases of mild inflammation, the hyperemia is very striking. Areas of extravasation of red blood-cells occur frequently in the mucosa. The occurrence of pigment has not infrequently been described even in the infant appendix. Hyperemia and small hemorrhages were naturally most marked in instances in which thrombosis was found in some of the arteries in either the wall of the appendix or the mesentery. When thrombosis was present, the mucosa and submucosa in places histologically suggested the picture of infarction with a secondary infiltration of the wall of the appendix with inflammatory cells. Thrombosis of blood-

7. Aschoff: *Die Wurmfortsatz Entzündung*, 1908, p. 8.

8. Obendorfer: *Ergebn. d. Allg. Path. u. path. Anat.*, 1909, xiii, 1, p. 553.

vessels elsewhere in the body has been observed at times in marantic infants; such a condition of the renal vessels is not uncommon. The condition of thrombosis in the appendices of these infants, as in the adult appendicitis, is probably the result of the blood-vessels of the appendix sharing in the adjacent inflammation. The inflammatory changes that are obvious, occur chiefly in the muscularis and serosa. The presence of polynuclear leukocytes, lymphocytes, and occasionally eosinophils, in a moderately edematous muscularis and in the strikingly edematous serosa, is the usual microscopic finding. The changes near the mesentery are perhaps most marked. The lymph-vessels are greatly distended with leukocytes and lymphocytes. The blood-vessels are greatly engorged and show the presence of many leukocytes and lymphocytes close to the intima, and in some cases actual thrombi. Sections of adjacent lymph-glands made in several cases, gave the usual microscopic evidence of acute inflammation.

It is of interest to note that the sections of the wall of the cecum or ascending colon made near the origin of the appendix, in only two instance in 200 cases showed inflammatory changes involving the intestinal wall. In both the cases the appendix was the site of inflammation. Hyperemia and hemorrhages into the mucosa occur not infrequently in these sections of the intestinal wall and at times small superficial necroses. In one case necrosis was seen in a lymph-follicle.

A hematogenous origin of appendix inflammation in such young infants is not probable. The early histologic picture in such infection in the adult appendix, according to Kretz,⁹ consists of small bacterial emboli seen in the capillaries of the lymph-follicles, together with small adjacent hemorrhagic exudates. Such lesions could not be demonstrated in the appendices described above.

Congenital syphilis was not found as an associated lesion in any of the fifteen infants. In two infants in whom congenital syphilis was believed to be a possible condition, based on the history obtained, the histologic findings in the viscera were entirely negative, and the *Spirochæta pallida* could not be demonstrated in the liver.

The extension of inflammation through a possible infection of the genital tract, as in Case 2, could be excluded by the microscopic findings. The serosa of the uterus and that of both tubes appeared intensely inflamed, while the muscularis and the mucosa were quite normal.

The cause of the inflammation must be sought for in the intestinal tract. In all probability the inflammatory changes in the appendices of young infants dying from malnutrition may be construed as a final infection of the appendix occurring in the later stages of a general infection of the gastro-intestinal tract.

9. Kretz: Verhandl. d. deutsch. path. Gesellsch., 1910, p. 147.

SUMMARY

1. Among 200 infants dying with gastro-intestinal symptoms and malnutrition, fifteen gave evidence at autopsy of inflammatory changes in the appendix.

2. The lesion occurred in infants whose ages ranged between 13 days and 2 months.

3. Peritoneal exudate was present in seven cases.

4. Thrombosis of the arteries occurred in the appendix and in the mesentery of the appendix in several instances.

5. The anatomic position of the appendix was found to influence the inflammatory changes.

6. The inflammatory changes in the appendices of young infants dying with symptoms of malnutrition occur probably as a result of a final infection of the appendices in the later stages of a general infection of the gastro-intestinal tract.

In concluding, I wish to express my obligations to Dr. John Howland for the privilege of performing the autopsies during his service as pathologist of the Foundling Hospital; and also to Dr. Eugene L. Opie, under whose direction the work was carried out.

PROGRESS IN PEDIATRICS

ANATOMY, PHYSIOLOGY AND HYGIENE

Continuous Function of the Mammary Glands

(Moriz Schein: *Wien. klin. Wchnschr.*, Sept. 22, 1910, *xxiii*, No. 38, p. 1337)

Schein believes that the mammary gland produces an internal secretion, of which we have had up to this time no knowledge; the function of the mammary glands is not periodic, but continuous. In those periods when milk or colostrum is not secreted, he believes that a varying quantity of an internal secretion is being produced insensibly.

MAURICE OSTHEIMER.

BACTERIOLOGY AND PATHOLOGY

The Incubation Period of Serum Disease

(F. Hamburger and R. Pollak: *Wien. klin. Wchnschr.*, August 11, 1910, *xxiii*, No. 32, p. 1161)

This forms the third communication made by the authors on this subject. After giving details of their experimental investigations, they conclude that there exists already, even during the incubation period of serum disease, a specific oversensitiveness to serum; and that this does not appear suddenly, but increases gradually in its intensity.

MAURICE OSTHEIMER.

Hemagglutinin Reaction in Serum Disease

(Felix Bauer: *München. med. Wchnschr.*, Jan. 10, 1911, No. 2)

Bauer tried to get a serum reaction which would be specific for serum disease. Such a reaction must be present in every case of serum disease and must also be present after any injection of serum without any signs of serum disease. He found that after any injection of horse serum there is a production of agglutinins in the blood. The technic is simple, being like that of the Widal reaction, except that washed horses' red blood-cells are used instead of typhoid bacilli. Complete agglutination occurs in dilutions of 1 to 200, or more, in pronounced cases of serum disease. This reaction would be of use in making a differential diagnosis of the skin condition in serum disease and the exanthemata.

HERMAN SCHWARZ.

Influence of the Components of Breast-Milk on the Intestinal Flora of Sucklings

(H. Bahrdt and A. H. Beifeld: *Jahrb. f. Kinderh.*, *lxxii*, Supplementary No. 71)

The authors, after reviewing the literature on *B. bifidus* and the intestinal flora of infants, report the results of microscopic examinations of stools of infants fed on various modifications of breast-milk, by which the influence of each constituent—fat, proteid, sugar, and salts—by its presence or absence, could be observed on *B. bifidus* of Tissier, present in the normal stool of the breast-fed infant, to the practical exclusion of all other organisms. Both centrifugalized human-milk, and breast-milk to which human-milk cream had been added produced stools in which the microscopic picture was identical with that of the breast-fed infant. This indicated that the fat played a minor rôle in determining the presence of *B. bifidus* in the stool. A suspension of human milk-curd in water, however, caused a disappearance of the *B. bifidus* flora, which was replaced by

the mixed—Gram-positive and negative—flora seen usually when cow's-milk mixtures are given. The whey, on the other hand, caused the reappearance of the bifidus flora, the same microscopic picture persisting after feeding a suspension of curd in a whey diluted with an equal part of water. The curd suspended in a still more dilute whey—three-fourths water—again permitted a large number of Gram-negative organisms to make their appearance. Suspensions of human as well as of cow's-milk curd in a 6 per cent. lactose solution gave a typical breast milk stool, with the corresponding bifidus flora. The conclusion is drawn that lactose is that constituent of human milk which is responsible for the exclusive presence of *B. bifidus* in the stools of the breast-fed infant. This is due to the fact that the relatively large quantity of this sugar, as against the slight amount of proteid, favors the normal fermentative process in the small intestine, the acid products of which (i. e. lactic acid) inhibit the growth of Gram-negative putrefactive bacteria, such as *B. coli*, which would flourish were the proportion of carbohydrate and proteid reversed. The Gram-positive bacteria such as *B. bifidus* and *B. acidophylus* are not checked in growth by the acid medium.

G. L. MEIGS.

METABOLISM AND NUTRITION

Cretinism Among Jews

(Arnold Flinker: *Wien. klin. Wchnschr.*, Dec. 29, 1910, *xxiii*, No. 52, p. 1871)

Flinker found fourteen cases of, apparently, endemic cretinism in Wiznitz, occurring among the Jews of the vicinity. He describes four of the patients in detail, with photographs. At the same time several cases were also found among others living in the neighborhood. While endemic goiters appeared in the first generation of settlers, cretinism was found in the second generation. No other children in the families of these children developed the disease, even though they lived and slept with the cretins all their lives. Flinker concludes that cretinism cannot, therefore, be contagious.

MAURICE OSTHEIMER.

Nitrogen and Sulphur Metabolism in Rachitic Dwarfism

(Herman Schwarz: *Jahrb. f. Kinderh.*, 1910, *lxxii*, Series 3, *xxii*, No. 5)

In the normal metabolism of a 5-year-old child, seventy calories per kilo weight was enough to cause an increase in weight in the seven-day experiment. In the first case of rachitic dwarfism, ninety-four calories per kilo, in the second case, ninety-four calories per kilo, and in the third case eighty-three calories was sufficient to keep them in nitrogen equilibrium and slightly increase their weight. The nitrogen resorption was 90 per cent. in the normal case, 93 and 96 in cases 2 and 3, and only 80 per cent. in case 1. The total nitrogen excretion in the urine in the normal case was 74 per cent., 72 per cent in case 1, 78 per cent. in case 2, and 81 per cent. in case 3. During a period of fever in case 2, the nitrogen excretion was increased. The ammonia nitrogen coefficient was about the same in all cases. During an attack of urticaria in case 1 the ammonia excretion was slightly increased, and during the fever attack of case 2 it was greatly increased. Uric acid nitrogen in the normal case was about 83 mg. per day, less in cases 1 and 2, and much less in case 3. The creatinin nitrogen excretion in the normal child was about 150 mg. The creatinin nitrogen coefficient was about 6.8. In cases 1 and 2 the creatinin was distinctly diminished, the coefficients being 5.9 and 2.4. This decrease might be due to a diseased condition of the liver. Creatin was not present in the normal case. In cases 1 and 2 the amount of creatin was often as much, if not greater than, the creatinin. This might be due, first, to a diseased condition of the liver (Mellanby), and second, to the condition of the musculature in these cases of rickets (Hagenbach-Burchardt and Bing). In case 3, in which the liver was normal in size and the child's locomotion

normal, there was no creatin excreted. The sulphur metabolism showed a resorption of 92.2 per cent. in the normal case, 76 per cent. in case 1, and 83 per cent. in case 2. The retention was 31 per cent. in the normal case, 30 per cent. in case 1, and 26 per cent. in case 2. The total sulphur excreted in the urine was 61 per cent. of the intake in the normal case, 55 per cent., 54 per cent. and 54 per cent. in cases 1, 2, and 3, respectively. The amount of sulphur in the feces was 7.8 per cent. of the intake in the normal case, 23 and 17 per cent. respectively in cases 1 and 2.

HERMAN SCHWARZ.

Two Methods of Obtaining Human Milk for Hospital Use

(Fritz B. Talbot: *Boston Med. and Surg. Jour.*, 1911, *clxiv*, 304)

The author describes the methods used to procure breast-milk at the Massachusetts Infant Asylum and the Boston Floating Hospital. At the former institution there are resident wet nurses, obtained from lying-in hospitals and other charitable institutions. These women take entire care of their own babies and do some light work. The milk of these wet nurses is used in two ways: (1) The milk is drawn with breast pumps for the very weak and delicate babies; (2) the stronger babies are put on the breast. The women are paid according to the amount of milk they supply, at the rate of two cents an ounce for "drawn milk" and one cent an ounce for nursed breast milk, up to a limit of sixteen dollars a month. Each woman gives about one quart daily. The average duration of residence in the hospital is six to eight months.

At the Boston Floating Hospital breast-milk was obtained by a trained nurse from nursing women in the tenement district who had a superabundance of milk. Mothers willing to supply milk were examined by one of the physicians of the hospital for signs of tuberculosis or syphilis. Each woman's family physician was then required to sign a card stating that in his opinion it would do no harm for the woman to supply this milk. The women were paid at the rate of sixty cents a quart but the movement became so popular that many of the mothers were unwilling to accept any recompense.

RICHARD M. SMITH.

Technic of and Indications for Feeding Albumin Milk

(H. Finkelstein and L. F. Meyer: *München. med. Wchnschr.*, Feb. 14, 1911, No. 7)

After describing the general procedure adopted at the Kinderasyl, Finkelstein and Meyer lay down the following rules to be observed in giving eiweissmilk:

1. The eiweissmilk must not have any lumps and on shaking should be of homogeneous consistency. From the start there must be at least 1 per cent. of carbohydrate, best in the form of a malt sugar.

2. In dyspepsia and atrophy (decomposition) a cathartic should be given, six hours tea diet, and then eiweissmilk in no smaller dose than 300 gm. a day—to which in most cases the 1 per cent. carbohydrate has been added. This is increased rather rapidly so that the child is given 180 to 200 gm. per kilo weight regardless of the character of the stools or other conditions. Should the weight not stop decreasing in the course of a few days, the carbohydrate must be increased to 2 to 3 per cent., especially when subnormal temperature and collapse occur. If the above named dose has been reached and there is no increase in weight, the carbohydrate is to be increased to 3, 4 or 5 per cent., or flour may be added instead. Many children do not gain until 6 or 7 per cent. carbohydrate has been added. As carbohydrate, dextrin-maltose preparations or flour alone or in combination are preferred.

3. Carbohydrate may be added even when the stools are numerous and watery up to 3 per cent. and, under close observation, even higher than this.

4. Under no circumstance should the carbohydrate be reduced below 2 or 3 per cent. when adding the carbohydrate has once been started.

5. Should untoward results occur during the administration of the eiweissmilk and the weight not decrease too rapidly, do not stop it but wait. Usually spontaneous improvement occurs. It is advisable to cut down the carbohydrate percentage slightly if it happens to be over 4 per cent. If marked decrease in weight

occurs it is best to cut down the amount of eiweissmilk from 150 to 200 gm. per diem and the carbohydrate to 2 or 3 per cent. All in all, until the intercurrent infection has disappeared it is best to give a little less than the 180 to 200 gm. per kilo and to stick to the 3 per cent. carbohydrate.

In enterocatarrh and cholera infantum they advise tea diet for twelve to twenty-four hours; then ten times, 5 to 10 gm. eiweissmilk and tea for the next twenty-four hours; then 50 gm. eiweissmilk are added daily until marked diarrhea has stopped; then a rapid increase to 180 to 200 gm. per kilo weight.

At this time they begin increasing the carbohydrate; should, however, the decrease in body weight not stop after three or four days of the treatment, the carbohydrate should be added earlier. In very toxic cases the above scheme should also be carried out. After giving 130 to 150 gm. eiweissmilk with 3 per cent. carbohydrate, one can wait until all toxic symptoms have disappeared. To try to reduce the toxemia by continued starvation is an error and can cause death. In conclusion they expressly state that no other nourishment should be given during the eiweissmilk therapy. Not even woman's milk should be added. In mild cases the addition of woman's milk has seemed to be without harm, but in serious cases it was distinctly deleterious.

HERMAN SCHWARZ.

ACUTE INFECTIOUS DISEASES

The Spread of Scarlet Fever

(*Heinrich Kokall: Wien. klin. Wchnschr., Dec. 29, 1910, xxviii, No. 52, p. 1874*)

Kokall relates histories of twenty instances of "return" cases of scarlet fever occurring just as soon as the apparently well child mingles with other children, in spite of disinfection repeated several times, isolation in the hospital, and even longer separation from the family and friends. He believes that disinfection is of no value in preventing these "return" cases; that the patient alone is the infecting agent, even for a long time after his attack; certainly longer than six weeks afterward. Therefore, efforts should be made to keep the mouth free from germs before letting a child out of quarantine. But no certain method has yet been found, nor will be, probably, so long as the exciting cause of scarlet fever remains unknown.

MAURICE OSTHEIMER.

Antityphoid Inoculation as Introduced into Certain Training Schools for Nurses

(*Mark W. Richardson and Leslie H. Spooner: Boston Med. and Surg. Jour., 1911, clxiv, 8*)

The authors report the inoculation of physicians, nurses and ward-tenders at the Massachusetts General and nine other hospitals in Massachusetts. This work was undertaken because from previous investigations it was concluded that "the hospital nurse in Massachusetts is about eight times as liable to contract typhoid fever as the ordinary citizen." Four hundred and five individuals were given 1,588 inoculations. There were no untoward results. At the Massachusetts General Hospital for the ten years previous to 1909 from two to six nurses had typhoid fever each year. In 1909 and 1910 there were no cases of typhoid fever among nurses in that institution. The authors believe that the inoculated individuals have acquired an increased resistance to typhoid infection which will last them for several years.

RICHARD M. SMITH.

TUBERCULOSIS AND SYPHILIS

Diagnosis of Tuberculosis of the Bronchial Glands

(*Henry F. Stoll. Am. Jour. Med. Sc., January, 1911*)

The author gives a careful résumé, with citation of authorities of the significant symptoms and physical signs leading to a diagnosis of this condition.

The points on which different observers lay greatest stress are: tenderness over the spines of the upper thoracic vertebræ; dullness over the fifth or sixth dorsal spines; paravertebral dullness, best elicited by light percussion; bronchophony downward over the thoracic spines for a variable distance, at times present only over the fifth; crepitant râles in the fourth, fifth and sixth interspaces at about the mid-clavicular line, and radiography. He points out the importance of a tuberculin test if one or more of the above signs are present. The author insists on the importance of early diagnosis as tuberculin therapy is most efficacious in glandular tuberculosis. The cases studied by Stoll were mostly in older children but he considers the points of diagnosis equally applicable to infants.

FREDERIC H. BARTLETT.

The Splenomegaly of Inherited Syphilis

(F. P. Weber: *Proc. Roy. Soc. Med.*, 1911, iv, 67)

Weber sums up his conclusions in regard to splenomegaly in children and inherited syphilis, from a study of the literature and six of his own cases, as follows: 1. Moderate splenomegaly in children from the ages of 5 to 16 may be almost the only evidence of an inherited syphilitic taint, but in such cases the Wassermann test would doubtless give a positive result. Other evidences of inherited syphilis are occasionally forthcoming, as Hutchinson teeth, interstitial keratitis, cracks at the corners of the mouth, a history of skin eruptions in babyhood, a history of syphilis in the parents, inherited syphilis in brothers and sisters, etc. 2. It may be accompanied by occasional slight attacks of jaundice and by excess of urobilin and urobilinogen in the urine. 3. Hepatic cirrhosis. 4. Infantilism—more or less retardation in physical development, especially in the sexual function. 5. In certain cases, a polycythemia, probably of a reactive nature. 6. Abdominal crises of uncertain explanation. Familial splenomegaly, occurring in two or more brothers or sisters. 7. Some cases present the symptoms of splenic anemia or Banti's disease.

J. B. C.

Pemphigus Syphiliticus of the New-Born

(Prof. Baisch: *München. med. Wchnschr.*, Jan. 31, 1911, No. 5)

Baisch describes a case of pemphigus syphiliticus which was observed in the Kgl. Universitäts Frauenklinik, München, and points out the bad prognosis in this form of congenital syphilis, even if given mercurial treatment. The spirochetes are always found in the serous contents of the bullæ and are more easily stained with carbol water gentian-violet than with Giemsa. The child was literally covered with pemphigus lesions, weighed 2,450 gm., and was 46 cm. long. Since Taege (*München. med. Wchnschr.*, 1910, No. 33) and Dubot (*München. med. Wchnschr.*, 1910, No. 35) pointed out the good effect on the infant of the injection of salvarsan into the mother, he injected 0.4 gm. into the cubital vein of the mother on the first day post partum. The mother nursed the child on the fourth day, yet during these days the lesions in the child did not increase. On the seventh day, however, many new bullæ appeared. On the eighth day the child received 0.15 gm. salvarsan in the gluteal region. The result was excellent; for on the ninth day the lesions had almost all dried up and the child increased in weight. On the eighteenth day new pemphigus lesions appeared and the child received another dose of 0.15 gm. These new lesions promptly disappeared and the child continued to gain weight and appeared perfectly well on the fortieth day.

HERMAN SCHWARZ.

The Effect of Ehrlich's Salvarsan On Lues in Children, Especially on Congenital Syphilis

(Richard Kalb: *Wien. klin. Wchnschr.*, Sept. 29, 1910, xxiii, No. 39, p. 1378)

Kalb reports the histories of eight children, two of whom had acquired syphilis, while six had hereditary syphilis. At first he employed small doses of salvarsan in neutral suspension, injected into the gluteal region. Later he used it in solu-

tion, supplied in sterile ampullæ. All the children stood the injections well, without pain or infiltration following. One child was suffering from Parrot's pseudoparalysis; another had great enlargement of the liver. Recovery occurred in the two children with acquired syphilis exactly as it occurs in adults. Mucous patches disappeared first, followed by the eruption, and last to go were the enlarged glands. In congenital syphilis the eruption disappeared first, then the bony changes and pseudoparalysis. While coryza may disappear rapidly, it may also persist for some time. In one child a defect of hearing improved very rapidly also. Kalb advises giving salvarsan to the nursing mother for its effect on the baby. He concludes that not only is salvarsan a more certain and more rapid therapeutic agent than any of the older methods of treating syphilis, but it may readily be employed in treating atrophic infants with severe gastric catarrh; it seems to increase body weight and improve the general condition of the infant.

MAURICE OSTHEIMER.

An Examination of Scrofulous Children by Means of the v. Pirquet and Wassermann Tests

(*R. Hertz and O. Thomsen: Berl. klin. Wchnschr., xliii, No. 6*)

The object of this work was to more surely establish, by means of a specific reaction, the fact that tuberculosis is a dominating factor of etiology in scrofulosis. Of 228 cases, 84 per cent. reacted positively to the v. Pirquet test, and 16 per cent. were negative. As all the cases were admitted to the Kysthospital for tuberculous surgical affections, this percentage is not remarkable; of the remaining 16 per cent., however, operation or autopsy proved the majority to be not tuberculous.

Wassermann tests on the 228 cases reacted positively in eight cases, of which four were only weakly positive; these four were later retested, and gave the same result. Three were evidently tuberculous, and one rachitic. These weak reactions showed only partial checking of hemolysis, and the same result was shown when the test was repeated several weeks later. Whether this meant luetic infection (congenital or acquired) must remain undecided, for such weak reactions have been known to occur in cases in which lues could most probably be excluded.

The mothers of these eight children denied all knowledge of having been infected with lues, and three of them were tested, with negative result; these three were manifestly tuberculous. Four showed marked positive reaction, and their children were given antiluetic treatment; undoubtedly in their cases the lues was the more serious factor of the illness; the marked Wassermann reaction, and the almost miraculous response to mercurial treatment, were clear.

Here is shown again the common experience, that the Wassermann test in congenital lues remains obstinately positive, even when combated vigorously with mercurials, and even if all symptoms disappear—a contrast to the behavior of acquired lues.

A. C. SOPEL, JR.

BLOOD AND CIRCULATORY SYSTEM

Arterial Rigidity in Children

(*Franz Hamburger: München. med. Wchnschr., Jan. 31, 1911, No. 5*)

Hamburger says that the temporal or radial artery should not be felt normally either in the adult or the child. He finds them often palpable in children above the sixth or seventh year—sometimes as young as the third year. At times they are so marked that one might think of an arterial sclerosis or a kidney condition, but there is no anatomic evidence of the former and no clinical evidence of the latter. Careful examination of these children show them to be of a neuropathic type. They complain of headache, cardiac palpitation, migraine, and vasomotor disturbances, such as cold hands and feet. He often finds a pulsus irregularis respiratorius.

HERMAN SCHWARZ.

Splenic Anemia

(A. Longo: *Médecine des Enfants*, December, 1910)

Longo has had in his clinic at Catane a boy 17 months old suffering from splenic anemia. Both of his parents are healthy; three other children living and well; one brother died. The boy was born at full term; was breast fed, and after the tenth month weaned. When 16 months old (middle of January) he suffered from green diarrhea, fever and pallor. The large spleen, somewhat enlarged liver, temperature and pulse of 124 at first suggested Malta fever. On February 19 the child was worse, looked extremely pale, and had gingivitis, with fetid breath. He died February 27, forty days after the onset of the disease. On February 20 the spleen was punctured and corpuscles of Leishman were found. Blood-count the same day showed, red cells 3,800,000; leukocytes 16,000. Serum tests for typhoid, paratyphoid and Malta-fever were negative.

J. BLECHSCHMIDT.

Infantile Splenic Anemia

(G. Zamboni: *Médecine des Enfants*, December, 1910)

In his article published in *Riv. di Clin. Pediat.* (July 10, 1910), Dr. Guiseppe Zamboni expresses it as his opinion that there is a fundamental difference between splenic anemia and kala-azar (Leishman). He refers to twelve of his patients treated at the pediatric clinic of Dr. C. Comba in Bologna.

These cases—several of which were treated by x -rays—showed the following variations in blood-counts: red cells, from 1,500,000 to 3,940,000; leukocytes, from 3,000 to 34,500. Pallor and splenic enlargement were dominant features, but fever was not constantly observed. (In kala-azar fever is present and a slight icterus usually accompanies it). Of his twelve patients, six died, two were cured (?), one slightly improved, one was of the adult form, two had unknown terminations.

Out of 146 published cases ninety-nine were boys, forty-seven were girls. Of the twelve cases of Zamboni seven were boys and five were girls. As to age, fifty-seven were 1 year or under; between 1 and 2 years, sixty-five; over 2 years, twenty-four. Of Zamboni's patients four were 1 year or under; seven were between 1 and 2, and one was over 2. The predominance of the disease in early life seems to point toward digestive disturbances as an etiologic factor. To this there must be added according to the author, congenital syphilis, maternal diabetes, anemic predisposition running in families, rickets, enlarged bronchial glands, malaria, measles and suppurative foci. As regards pathogenesis, the spleen is of primary importance and by acting on it, x -rays combat the anemia. In none of his cases has Zamboni been able to discover the parasites of Leishman.

J. BLECHSCHMIDT.

Hemophilia and Blood Coagulation

(Max Vogel: *Ztschr. f. klin. Med.*, 1910, p. 224)

Vogel reports a case of hemophilia in a 10-year-old boy in whose family for three generations back no history of hemophilia could be traced. The parents of the boy were blood relations (cousins). At 6 months of age he suffered from a subcutaneous hemorrhage. When 11 months old he received a slight injury to the frenum of the tongue, which was followed by hemorrhage that lasted eleven days, and it was at this time that the diagnosis was made. At various times it was noticed that slight injuries caused marked hemorrhages, external or subcutaneous. In 1907, hemorrhages into the knee and ankle joints were first noticed. Since this time the general health declined and there were also hemorrhages into both knees. The patient became bedfast; every attempt to arise being associated with severe pains and copious hemorrhages into the knee-joints. The boy was under Vogel's care for about a year and a half, during which time there had never been any hemorrhage into the mucous membranes. Nov. 20, 1909,

the boy's condition was especially marked by lameness from the affection of both knees. His development indicated a fairly well nourished boy (weight not stated). The skin and mucous membranes were somewhat pale. On the left temple there was a prominent scar (4x3 cm.). Other scars were found on front of the left thumb, and on the lips. There was a subcutaneous hematoma in the right popliteal space. Both knee-joints were considerably swollen and fluctuating and were painful on motion. Radiographs showed normal bones; there was no edema; temperature, heart and lungs normal; urine without special interest; liver and spleen normal; a few indolent glands the size of hazel nuts, in the inguinal region. Hgb. 70 per cent.; r. b. c. 5 million; whites 8,500. Since November 9, the condition of the boy did not change materially and he had been unable to leave his bed. About the joints, spontaneous hemorrhages would occur, here and there.

This condition should be differentiated from congenital hemophilia, in which there is bleeding from the mucous membranes and internal organs (nose, kidneys, bowels, etc.). It may also be added that the progress of the hemorrhagic lesions in this case was very slow.

The coagulation of the blood was tested by Vierordt's and Morawitz's methods. By Vierordt's method, normal blood coagulates in four hours; hemophilic blood in thirteen hours ten minutes. By the Morawitz method normal blood coagulates in five hours thirty minutes; hemophilic blood in eighty-eight hours and forty-five minutes.

The blood of three brothers of this patient was tested by the Vierordt method and gave the following results: (1) seven hours fifteen minutes; (2) seven hours forty-five minutes; (3) twenty-one hours twenty-five minutes. As a control test, the blood of a healthy stranger coagulated in seven hours twenty-five minutes. It is interesting to note that the third brother, although not a bleeder, had blood with hemophilic coagulation time.

Vogel made coagulation tests of the blood with various materials, as organic extracts, fresh serum, diphtheria antitoxin, calcium chlorid, phenol, glycocoll, grape sugar and fresh human and rabbit's blood. He found that a clot was readily obtained by adding human and rabbit's blood; with the other tests, the blood was still fluid after twenty-four hours.

By adding 2 c.c. rabbit-blood to 3 c.c. joint-blood a clot was obtained in seven hours fifty-five minutes, but by adding seven drops human blood to 2 c.c. joint-blood a clot was only established after sixteen hours thirty minutes. Very marked was the uselessness of the organic extracts. Under the impression that the result could be improved by adding lime salts to organic extracts, calcium chlorid and organic extracts together were tried, but again with absolutely negative results. A control test with normal blood and rabbit's blood proved the rapid, strong reaction, a clot being formed in fifty minutes.

Perhaps all these tests do not prove conclusively the correctness of Sahli's hypothesis concerning hemophilia. In conclusion Vogel considers this a new case of hemophilia in which clotting took place in eighty-eight hours (Morawitz-Bier method). Experiments with this method gave slight reaction with glycocoll. Sodium chlorid always acted slowly. Fresh-flowing rabbit's blood always worked rapidly. Organic extracts also hastened very much the clotting of normal blood. In rabbits intravenous injection of organic extracts made very little impression. Hemophilic blood mixed with organic extracts under the same condition will flow after one hour like normal blood. Lastly, Vogel calls attention to the third brother of the patient, whose blood coagulation time was the same, although never having had any evidences of hemophilia.

C. H. LEFCOE.

Splenic Anemia a Parasitic Disease

(*R. Jemma: Médecine des Enfants, December, 1911*)

Italian pediatricians (Cardelli, Somma, Fede) had for a long time considered splenic anemia as a disease distinct from other splenic enlargements. What their clinical observations led them to surmise has just been demonstrated with a cer-

tain precision by Dr. Rosco Jemma, professor of Pediatrics in the University of Palermo.

Searching for the parasite of Leishman in cases of splenic anemia he punctured the spleens of these patients, but was at first unsuccessful. Later, in May, 1909, he found the parasites in a boy aged 6. He was healthy up to his fifth year; the disease began in January, 1909, with fever preceded by chills and followed by sweats. The fever continued for three months and was irregular in every way; i. e., as to time of attacks, duration and intensity. In the beginning it was of the quotidian type; later it was absolutely irregular. There was nausea, dry cough, with pain in the left hypochondrium, headache, pallor of skin and mucous membranes, emaciation, no enlarged glands, but protruding abdomen, enlarged liver and spleen, the upper border reaching the eighth rib; the lower border 3 cm. below the transverse umbilical line. Blood-count May 1 was as follows: erythrocytes, 3,000,000; leukocytes, 16,000; hemoglobin, 65 per cent.

Puncture of the spleen in June gave a negative result. Tests for typhoid, paratyphoid, Malta fever and Koch's bacillus were all negative. The fever continued with light remissions and periods of the intermittent type to the end of August. Attempts were made to build the child up. X-rays brought some amelioration. The blood-picture September 20 showed: reds 3,987,000, whites 11,870, hemoglobin 65 per cent. October 3 another splenic puncture was made by means of a special trocar which allowed withdrawal of some of the splenic pulp. Preparations of this with Giemsa stain showed the corpuscles of Leishman, which the latter found and described in patients suffering from kala-azar in India, and which later on were found by Nicolle (Tunis) and by Pianese and Gabbi (Italy), in individuals attacked with splenic anemia. There can be no doubt that the enlargement of the spleen and all the other symptoms of the disease in this boy were due to these parasites. They were not found the first time because a Lür syringe with an ordinary needle was used; the special trocar used the second time allowed some of the splenic pulp to be withdrawn. Jemma is convinced that many of the cases of infantile splenic anemia which he has observed in hospital and private practice are due to the parasites of Leishman. In an article in *Riforma medica* (1910) he has described six additional cases of infantile splenic anemia in which he was able to demonstrate the presence of the Leishman corpuscles after splenic puncture. It is remarkable that in one case he succeeded in inoculating a dog with it.

Sir Patrick Manson defines kala-azar as an infectious disease characterized by its chronicity and irregular fever, hypertrophy of the spleen and often of the liver, the presence of Leishman corpuscles in these and other organs, emaciation, anemia, frequently a peculiar pigmentation of the skin and a high mortality. Nearly all of these symptoms were found in Jemma's observations. The cases of kala-azar studied in India by Leishman and Donovan have often been attributed to malarial cachexia, but the corpuscles discovered by these two scientists have removed all doubts. In the human body these parasites are nearly always intracellular; they multiply in the invaded cell until it bursts and then they attack other cells. The disease is probably transmitted by the sting of an insect.

Kala-azar attacks both sexes, all ages, the natives as well as the new-comers—contrary to malaria. According to Roger there is only a moderate degree of anemia and there is leukopenia. In all the cases reported by Jemma there was slight leukocytosis. The inoculation of dogs was successful in Tunis (by Nicolle) and in Palermo (by Jemma); the corpuscles of Leishman were found in the spleen of these animals. Nicolle even thinks now that children might be infected by dogs. He has tried to prove the existence of a spontaneous infection of "Leishmania" in the Tunis dogs. Post-mortem examination of twenty-five dogs showed corpuscles of Leishman in four of these animals. Therefore, in Tunis, kala-azar might be of canine origin.

Following in the steps of Nicolle, Dr. Jemma examined the spleen of 170 dogs in Palermo with negative results. However, the parasite of Sicily has been identified by Dr. Nicolle with that of Tunis. The kala-azar of Palermo is there-

fore the same disease as that of Tunis. The cultures of the parasite on different media, especially agar, have given positive results (although very slowly and with difficulty). The conclusions are as follows:

There is no doubt that there exists in Palermo as in Naples, Messina, Catane, an infectious disease caused by a parasite which by its morphologic and cultural characteristics resembles that which Leishman has found in Indians attacked with kala-azar. But we cannot yet admit the identity between the Indian kala-azar and the infantile splenic anemia of Tunis or Sicily. In India the kala-azar (or dum-dum-fever) takes an epidemic or endemic form and has a high mortality. In Italy splenic fever or splenic anemia—although considered an infectious disease by different authorities (Fede)—has never shown an infectious or epidemic character. In India kala-azar attacks all ages; in Italy splenic anemia is limited to young children. The cutaneous pigmentation of Indian kala-azar is not seen in infantile splenic anemia. In India the disease develops with a fever more or less intense, lasts some months, is nearly always fatal. In Italy it is sometimes without fever, may persist for several years, and often ends in recovery.

Nicolle and Jemma have been able to raise the parasite on agar; in India it grows only on a specially prepared blood-serum. In Italy and Tunis it is inoculable in dogs; in India it is not. Therefore, for the present one cannot consider that these two diseases are identical.

Pianese, who was the first to show in Italy the presence of Leishman corpuscles in infantile splenic anemia, continues to distinguish two forms of the disease: (1) The parasitic form, due to Leishman's corpuscles; (2) that due to different causes, such as syphilis, tuberculosis, malaria and diseases of nutrition.

One must understand that infantile splenic anemia (so well described by Cardarelli, Somma, Fede) is a primary disease which has nothing to do with syphilis, tuberculosis or malaria. From now on one ought to reserve the name of splenic anemia for the disease characterized by the presence of Leishman's corpuscles. The other varieties ought to be called splenomegaly with secondary anemia due to syphilis, tuberculosis and malaria.

Kala-azar, says Dr. Jemma in closing, is a tropical disease which has nothing to do with our infantile splenic anemia, although the causal protozoa of these two diseases have very similar morphologic characteristics. We leave the exotic term (kala-azar) to the Indian disease and continue to call the other disease splenic anemia, under which name it has been known and described for generations.

J. BLECHSCHMIDT.

GENITO-URINARY DISEASES

A Superfluous Ureter

(Robert Cristofetti: *Wien. klin. Wchnschr.*, Oct. 27, 1910, *xxiii*, No. 43, p. 1510)

Cristofetti reports an interesting case of a girl aged 15, who had been treated for years unsuccessfully for incontinence of urine. He found that she had a third ureter which opened into the vagina. After trying unsuccessfully to operate through the vagina, he finally performed laparotomy, found the dilated extra ureter lying close to the normal left ureter, dissected it free and inserted it into the bladder anterior to the normal ureter. Cystoscopic examination four weeks after the patient had left the hospital showed urine entering the bladder through all three ureters.

MAURICE OSTHEIMER.

Infections of the Urinary Tract by *Bacillus Coli* in Infancy and Childhood

(C. R. Box. *Pediatrics*, *xiii*, No. 1)

In discussing infections of the urinary tract by the colon bacillus, Box summarizes treatment as follows: 1. The administration of sufficient potassium

citrate to make and keep the urine permanently alkaline. 2. Treatment by urinary antiseptics. 3. Treatment by serums and vaccines. In cases with acute local symptoms potassium citrate, administered in doses of 10 to 20 grains three or four times a day, has been entirely effectual. Urotropin and its allied antiseptics of the formalin group, also ammonium benzoate, sodium salicylate and boracic acid, were most disappointing, particularly in the chronic persistent cases. Serums were not needed in the acute cases. No permanent improvement was noted in the two chronic cases in which the patients were treated with autogenous vaccines, but incidentally it was discovered that washing out the bladder with the serum instead of urinary antiseptics produced a marked though temporary diminution in the number of bacilli present.

HENRY F. KEEVER.

Method of Collecting Urine from Female Infants

(Charles H. Lawrence, Jr.: *Boston Med. and Surg. Jour.*, 1911, *clxiv*, 309)

The method described is as follows: In a strip of adhesive tape, 2x6 inches, cut a hole a little larger than the vulval orifice of the infant from whom the specimen is to be obtained. The end of the strip which is to be applied posteriorly is split into two tails. A rubber glove thumb, cut off close to the glove, is dropped, tip first, through the hole in the strap, the adhesive side of which is held uppermost. That part of the rubber thumb which remains above the hole is turned down on to the adhesive surface of the strap and pressed firmly against it, care being taken to have the rubber flange narrow enough so that there will be a band of adhesive surface around it. The tip of the thumb is cut off, a test tube inserted and the joint made tight by wrapping it with adhesive tape. To apply the apparatus the strap is placed over the perineum so that the opening in it lies over the vulva, the anterior end extends up on to the lower abdomen while the posterior tails are directed backward and outward over the buttocks.

RICHARD M. SMITH.

Undeveloped Testicles

(Joseph Kyrle: *Wien. klin. Wchnschr.*, Nov. 10, 1910, *xxiii*, No. 45, p. 1583)

Kyrle has thoroughly examined testicles from 110 cadavers of boys under 18 years of age, thirty-nine of them from infants under 1 year of age. In thirty-one evidence of tuberculosis was found; twenty-nine of these having died under 9 months of age. Of the 110 individuals, eighty-six were decidedly undeveloped; of the rest, twenty-four did not show normal development for the age of the boy. Of the thirty-nine infants under 1 year, twenty-nine had undeveloped testicles. Kyrle considers the presence of a large amount of intracellular connective tissue between the testicular canaliculi a good sign of undevelopment. The presence of other congenital anomalies in many of these cases substantiates the possibility of this undevelopment being congenital also. In others it may have been the result of chronic or infectious diseases. He believes that a large number of boys must be born with undeveloped testicles. The fact that so large a number of those dying in infancy had undeveloped testicles would lead one to conclude that, associated with this lack of development, there was also a decided lack of vital resistance.

MAURICE OSTHEIMER.

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STUDIES ON INFANT NUTRITION

UNDER THE DIRECTION OF L. EMMETT HOLT, M.D., AND P. A. LEVENE, M.D.

*I. Metabolism in Chronic Malnutrition**

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Growth is the principal function of infancy, and any disturbance of it constitutes a serious condition. A state of nutrition which maintains the weight and size of the organism unchanged is desirable for the adult; it cannot be endured with impunity for any length of time by the infant.

Unfortunately disturbances of nutrition are not infrequent, principally among artificially-fed infants. The condition may follow some acute disease or may develop gradually as a result of some form of irrational feeding. It has been named differently by various writers at different times. It has been studied as atrophy, marasmus, simple wasting, decomposition, etc. But, notwithstanding the numerous investigations into its nature, and notwithstanding the many theories advanced for the explanation of the condition, the actual pathogenesis of the retarded growth of these infants still remains obscure.

In view of these considerations an attempt has been made to study the metabolism of infants in different phases of this condition. The difficulties of the undertaking were fully realized. In addition to those that are common to all metabolism work, there are additional factors arising from the technic of the investigation on infants. The position and restraint necessary in the metabolism apparatus, and even the surroundings of the hospital, affect the general health of an infant much more than the usual routine of a metabolism experiment affects the adult.

However, it was hoped that a careful study of a considerable number of patients, extended over a long period of time, would furnish information which might serve to establish a rational treatment of these disturbances. The patients on whom these studies have been made were all inmates of the Babies' Hospital, and for the most part they were admitted for disordered nutrition. The clinical details have been carried

*From the Laboratories of the Rockefeller Institute for Medical Research, and the Babies' Hospital, New York.

out by Dr. Josephine Hemenway, resident physician of the Babies' Hospital.

The present communication may be regarded as preliminary and contains a report on metabolism experiments on seven infants. The age of the patients varied from 3 to 7 months, and the duration of the observation from 3 to 106 days. The last represents the longest metabolism experiment on an infant thus far recorded. Attention has been paid to the nitrogen metabolism, fat metabolism, and to a certain extent to the mineral and water balance.

The food analysis was made in every experiment.

METHODS OF ANALYSIS

Total nitrogen in food mixture, urine, and dried feces was determined by the Kjeldahl-Gunning method.

Ammonia nitrogen was determined by the Folin method.

Sugar was determined by Pavy's method.

Starch when present was first hydrolyzed by heating with dilute sulphuric acid in an autoclave, and the sugar thus formed titrated according to Pavy.

Fat estimation: In order to determine the total fatty acids, food mixtures or feces were evaporated to dryness on a water-bath. Samples of the dry residues were thoroughly mixed with dilute phosphoric acid and the mixtures extracted in a Soxhlet apparatus with ether. In order to free the ethereal residues from moisture they were redissolved in chloroform, filtered through filter paper saturated with chloroform, and the weight of the chloroform residue determined. The neutral fat and free fatty acids were determined by extracting the dry samples of food-mixtures or feces with ether.

The total ash was obtained by igniting the dried feces and the residues from the evaporated urine with a few drops of concentrated nitric and sulphuric acid. The bases were calculated as sulphates.

Phosphoric acid was determined by titration with uranium acetate. For determination of phosphoric acid in the feces, the ash was dissolved in the smallest possible quantity of concentrated hydrochloric acid. An aliquot part of the solution was neutralized with sodium acetate and titrated with uranium acetate.

Calcium estimation was carried out in the usual manner. It was precipitated from solution by means of ammonium oxalate. The oxalate was transformed by ignition into the oxid. The calcium content of the urine was found too small to make possible an accurate determination.

The clinical histories of the patients are given at the end of the report. The results of the analyses are tabulated (Tables 1, 2 and 3).

The discussion of the results will be directed principally to the analysis of the peculiarities of nitrogen and fat metabolism. Carbohydrate, mineral and water balance will be discussed only in their effect on either protein or fat assimilation.

NITROGEN METABOLISM

A. General Considerations

Protein was regarded for a long time as the exclusive foodstuff on which depended the growth of the young. The utility of a foodstuff according to the views of those days, was determined principally by the digestibility of its protein material. These views, however, collapsed as soon as they were subjected to the experimental test. Rubner and Heubner have made it clear that fat and carbohydrates share equally with protein in their power to aid the maintenance and growth of the young as they do in maintaining the integrity of the adult. The law of the isodynamic value of these three principal sources of animal energy is applicable to all ages. Later investigations have demonstrated that in health practically every protein is equally well digested and absorbed from the intestinal tract of the infant; and further, it was established that in health, fat has an insignificant influence on the rate of absorption and assimilation of protein, while the influence in this direction of carbohydrate is very marked, exercising a protecting power over the combustion of protein and therefore increasing the degree of its assimilation.

Notwithstanding the revision in the view of the rôle of protein in the process of nutrition of the infant, it remains true that growth of tissues cannot take place without a retention of nitrogen in the organism. It is natural to find, therefore, that considerable attention was devoted to the study of nitrogen metabolism in conditions of malnutrition.

The earlier investigations into the nitrogen metabolism of atrophic children belong to Rubner and Heubner,¹ to Baginsky,² and to Bendix.³ In the patients of Rubner and Heubner and of Baginsky, protein assimilation was lowered. Baginsky reached the conclusion that infantile atrophy was caused by disturbed assimilation resulting from the atrophic changes in the gastro-intestinal tract.⁴ Also in the patient of Heubner and Rubner the absorption was apparently defective. Bendix was the first to make the observation that normal protein metabolism coexisted

1. Rubner and Heubner: *Ztschr. f. Biol.*, 1899, xxxviii, 360.

2. Baginsky: *Deutsch. med. Wchnschr.*, 1899, xviii, 281.

3. Bendix: *Arch. f. Anat. u. Physiol. Suppl. Vol.*, 1899, 206.

4. In this discussion the term "atrophic" will be abandoned, and the terms of Finkelstein—decomposition and intoxication—will not be made use of. All the various conditions that result in the retardation or the apparently complete arrest of growth will be referred to as infantile malnutrition.

TABLE 1.—AVERAGE DAILY FOOD INTAKE AND WEIGHT BALANCE

Period	Dates	Composition of Food	Volume of Milk c.c.	Protein Gms.	Carbo- hydrate Gms.	Fat Gms.	Weight Balance* Gms.
I. JAMES							
1	Nov. 18-22	 $\frac{1}{2}$ milk, 5% lime-water, barley-water to volume, 3 $\frac{3}{4}$ % milk-sugar additional	512	18.0	30.8	23.3	+36.8
2	Nov. 23-26	Same, except 5 5/7% milk-sugar	525	18.1	66.2	18.1	+46.0
3	Nov. 28-Dec. 1	60-60% skimmed-milk, 5% lime-water, barley-water to volume, 5% milk-sugar	578	19.4	51.4	10.7	-10.6
4	Dec. 8-16	55-65% skimmed-milk, 5% lime-water, concentrated barley-water to volume	651	25.0	39.3	14.9	+ 9.4
5	Dec. 18-20	65% skimmed-milk, 5% lime-water, conc. barley-water to vol., 12 c.c. Mellin's Food	651	24.0	54.3	18.3	+14.2
6	Dec. 22-24	Same, except no Mellin's Food	651	25.8	39.4	15.8	+18.9
7	Dec. 31-Jan. 3	 $\frac{2}{3}$ milk, 5% lime-water, water to volume	770	27.3	31.4	31.5	+60.2
8	Jan. 5-6	Same, but peptonized	770	26.0	29.7	27.0	-42.5
9	Jan. 9-14	 $\frac{3}{4}$ skimmed-milk, $\frac{1}{4}$ water, 3.08 gms. NaHCO ₃	880	28.0	33.7	12.1	+ 2.4
10	Jan. 22-24	 $\frac{1}{2}$ skimmed-milk (3 oz. off top), $\frac{1}{2}$ soy bean gruel, 2 gms. NaCl, 16 c.c. beef-juice	604	26.1	26.0	16.2	+55.6
11	Jan. 26-28	Same, except milk 4 oz. off top	604	26.3	27.6	7.9	-54.0
12	Feb. 19-24	 $\frac{1}{2}$ fat-free milk, $\frac{1}{2}$ soy bean gruel, 2 gms. NaCl, 32 c.c. beef-juice, 1.2% olive oil	508	24.9	23.0	14.2	-25.8
13	Feb. 25-Mar. 2	Same, except 1.6-2.0% olive oil	525	27.2	25.9	18.8	+ 5.2
II. DAKAK							
1	Mar. 8-11	Skimmed-milk, 5% lime-water, milk-sugar to 6%, 20 c.c. malt soup extract	1050	18.1	67.9	19.7	+48.5
2	Mar. 12-14	Same, except only 12 c.c. malt soup extract	641	10.8	38.2	12.3	+ 4.3
III. STOCKER							
1	Mar. 17-18	40% milk, 5% lime-water, barley-water to volume, 4 1/6% milk-sugar additional	415	15.2	60.4	17.0	+68.5
2	Mar. 19-20	Same, except milk-sugar only to 3%	418	15.3	38.2	18.7	+ 7.7

3	Mar. 23-24	Same, except no additional milk-sugar	462	16.6	29.2	22.4	-10.0
4	Mar. 26-27	Same, except 10 c.c. malted milk additional	462	16.1	32.9	16.3	+72.5
5	Mar. 28	Same as in Period 3	462	14.4	29.2	19.9	- 7.0
6	Mar. 29	40% milk, 5% lime-water, arrow-root gruel (2 drams to pt.) to volume	462	13.8	26.8	15.5	-12.0
7	Mar. 31-Apr. 1	35% fat-free milk, 5% lime-water, soy bean gruel (1 oz. to pt.) to volume	404	17.9	19.5	2.3	-80.5

IV. GUERIN

1	Apr. 13-16	45% milk, 5% lime-water, barley-water to vol., 2 13/16% milk-sugar additional, 16 c.c. malt soup ext., albumin of 2 eggs	473	25.5	50.3	17.9	+ 8.5
2	Apr. 18-25	Same, except 50% milk	479	27.0	51.5	22.5	+23.4
3	Apr. 27-29	Same with 6 c.c. olive-oil	479	26.9	49.1	29.8	-17.0
4	May 1-2	40% milk, 5% lime-water, barley-water to vol., 16 c.c. malt soup ext., albumin of 2 eggs, 8 c.c. olive-oil	120	23.5	47.7	25.5	- 1.0

V. FRANCO

1	May 7-10	40% milk, 5% lime-water, barley-water to volume, milk-sugar to 5%, 12 c.c. malt soup extract	414	16.0	60.6	15.8	+27.8
2	May 22-27	Same, with 4 gms. NaCl	420	15.5	55.0	14.0	+ 4.6
3	May 28-30	Same, except 5 gms. NaCl	417	15.7	54.1	12.9	+ 1.7

VI. VOGELIN

1	May 13-15	45% milk, 5% lime-water, barley-water to volume, milk-sugar to 5%, 12 c.c. malt-soup extract	473	18.2	56.3	15.0	-25.0
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VII. DOLAN

1	May 18-20	40% milk, 5% lime-water, barley-water to volume, milk-sugar to 5%, 20 c.c. malt soup extract, 6 c.c. olive-oil	420	16.3	57.1	21.8	-18.7
	May 18-19	to 5%, 20 c.c. malt soup extract, 6 c.c. olive-oil	420	16.8	57.1	22.3	-14.5
	May 20		420	15.1	57.1	20.8	-27.0

*By weight balance is meant average gain or loss per twenty-four hours.

with the condition of chronic malnutrition. Later similar observations were recorded by many writers⁵ on protein metabolism in infants.

B. Protein Absorption

Protein absorption generally is measured by the difference in the values of the nitrogen intake and of the nitrogen content of the feces. However, in recent years attention has been called by Orgler⁶ to the fact that the nitrogenous portion of the feces is composed not exclusively of the unabsorbed residue of the food nitrogen, but contains the nitrogenous substances of the intestinal secretions. Orgler, in fact, regards all the nitrogen of the feces as derived from the latter source. So long, however, as the source of the feces nitrogen is not as yet fully established, it was considered more conservative to estimate the value of protein absorption by the old method, bearing in mind that the values obtained in this manner are minimal.

It has been pointed out by Orgler that the nitrogen output through feces remains approximately constant, regardless of the nitrogen intake, although the value varies for every infant. The observations on our patients (Table 2) harmonize with this view. Thus, in Janes (Case 1) the nitrogen content of the feces was for only one day 0.23 gm. and for two days about 0.35 gm. each day. In the other periods, the output was about 0.40 gm. and only once reached 0.78 gm. Thus the value was not absolutely constant, though the fluctuations were not very great. It remained practically constant when there was little variation in the nitrogen intake. Thus in the three experiments on Franco (Case 5) the intake remained 2.56, 2.47, 2.51 gm. nitrogen per day of each period, and the nitrogen output for each of the three periods was 0.49, 0.48, 0.50 gm. The proportion of absorbed nitrogen varied in Janes (Case 1) from 80 to 91.5 per cent., the average being about 87.0 per cent. of the intake. In all other patients the absorption exceeded considerably 80 per cent. of the intake, with the exception only of Stocker (Case 3). In this instance the low average of nitrogen absorption of about 78 per cent. was conditioned by higher intestinal peristalsis. Thus, from the standpoint of protein absorption our patients presented little abnormality.

C. Nitrogen Balance

The nitrogen retention reached a higher value in those of our patients who showed a very considerable gain in weight in course of the experi-

5. Orgler: *Jahrb. f. Kinderh.*, 1908, lxvii, 383; *Monatschr. f. Kinderh.*, 1908, 135; Freund: *Jahrb. f. Kinderh.*, 1904, lix, 421; 1905, lxi, 36; Cronheim and Muller: *Biochem. Ztschr.*, 1908, ix, 76; Lange and Behrend: *Jahrb. f. Kinderh.*, 1897, xlv, 337; Philips: *Monatschr. f. Kinderh.*, 1906, 413; Meyer, L. F.: *Jahrb. f. Kinderh.*, 1910, lxxi, 379.

6. Orgler: *Ergebn. d. Inn. Med.*, 1908, ii, 464.

ment, and thus were in a state of convalescence. In Franco (Case 5), who was gaining weight continually, the nitrogen retention reached the high value of 41.8 per cent.; in Guerin (Case 4), who also showed a marked gain in weight during three experiments, the highest retention was 33.1 per cent. of the intake. On the other hand, in Janes (Case 1) no parallelism is noted between the curve indicating the gain in weight and that of nitrogen retention. Thus, during the period of the highest nitrogen retention of 1.091 gm. per day, the body weight showed no gain; and on the other hand in period 9, when the body weight reached the highest value of 4,680 gm., the nitrogen retention was only 0.552 gm. per day. However, most instructive is the consideration of the total nitrogen balance for the fifty-three days recorded in the tables. The total retention of nitrogen for the period was 34.53 gm. According to the analysis of W. Camerer,⁷ Jr., the nitrogen content of a new-born infant is 1.95 per cent. On the basis of this the nitrogen gain ought to correspond to 1.726 gm. The ultimate gain in weight was only 120.0 gm. Admitting that the value of Camerer is not absolutely correct, and that some of our values are not free from error, one nevertheless is impressed by the fact that during the time of the experiment there was undoubtedly a considerable growth of the mass of cellular material, without any marked increase in the body weight. It must be mentioned in this connection that Camerer has also noted a gain in the size of infants without a corresponding gain in weight.

FAT METABOLISM

A. General Considerations

According to the view of the majority of writers, the most striking manifestation of abnormal metabolism in infantile malnutrition is the response of the organism to the administration of fat. Fat added to the food of normal infants in quantities exceeding considerably the average requirement does not alter in any way the character of the general metabolism, may not cause any disturbance, and on the contrary may bring about a rise in the rate of daily gain in weight.

In infantile malnutrition the response is very different. The most obvious abnormality and, from the practical standpoint, the most important one is, that the increase in the fat intake causes a disturbance of digestion and a loss instead of an increase in weight. The abnormal "weight response" is associated with symptoms of general discomfort. This peculiar influence of fat in infants with chronic malnutrition has been the subject of numerous experimental investigations. Steinitz.⁸

7. Camerer, W., Jr.: *Ztschr. f. Biol.*, 1900, xxxix, 182; and *Ztschr. f. Biol.*, 1900, xl, 531.

8. Steinitz: *Jahrb. f. Kinderh.*, 1905, lvii, 689.

3	Mar. 23-24	2.65	1.86	.34	18.2†	.69	1.96	73.9	.10	3.7	5.0
4	Mar. 26-27	2.59	1.83	.36	19.9†	.56	2.03	78.2	.20	7.7	9.9
5	Mar. 28	2.30	1.71	.32	18.9†	.47	1.83	79.7	.13	5.4	6.8
6	Mar. 29	2.20	1.58	.33	20.7†	.68	1.52	69.0	-.07		
7	Mar. 31-Apr. 1	2.86	1.92	.30	15.0†	.65	2.21	77.6	.29	10.3	13.2
IV. GUERIN											
1	Apr. 13-16	4.08	2.22	.14	6.2	.68	3.40	83.5	1.18	29.1	34.8
2	Apr. 18-25	4.32	2.36	.15	6.3	.62	3.71	85.8	1.34	31.1	36.2
3	Apr. 27-29	4.31	2.11	.18	8.3	.77	3.53	82.2	1.43	33.1	40.3
4	May 1-2	3.76	2.12	.18	8.7	.68	3.08	81.8	.96	25.4	31.1
V. FRANCO											
1	May 7-10	2.56	1.00	.09	9.3	.49	2.07	81.1	1.07	41.8	51.6
2	May 22-27	2.48	1.36	.11	7.9	.48	1.99	80.7	.63	25.5	31.7
3	May 28-30	2.51	1.52	.12	7.9	.50	2.01	80.2	.49	19.7	24.6
VI. VOGELIN											
1	May 13-15	2.91	1.44	.16	11.2	.60	2.31	79.5	.86	29.7	37.4
VII. DOLAN											
..	[May 18-19]	2.69	1.59	.07	4.3	.31	2.29	88.2	.72	27.6	31.3
..	[May 20]	2.41	1.56	.08	4.8	.26	2.43	90.3	.85	31.4	34.8
1	May 18-20	2.60	1.58	.07	4.4	.40	2.01	83.7	.46	18.9	22.6

*Figures represent average values for twenty-four hours.

†Urine alkaline.

‡Urine acid.

Keller,⁹ Freund,¹⁰ Birk,¹¹ Rothberg,¹² and L. F. Meyer¹³ have furnished most valuable contributions in this connection. Special attention was paid by these authors to the mineral metabolism. But even after these recent contributions, the number of thoroughly described cases is not sufficient to permit establishing a clear causative relationship between the various symptoms observed in the course of this diseased condition. *A priori*, the ill effects of fat intake may be attributed to either one of the following assumptions:

1. Lack of absorption.

2. The effect of the fatty acids on the mineral metabolism. The presence in the intestinal wall of considerable quantities of soaps may lead to a deficient supply of mineral elements to the tissues.

B. Fat Absorption

In health comparatively little fat is removed by the feces, over 95 per cent. being absorbed from the intestinal tract. On this point most observers are in harmony. Less accord exists regarding the view on fat absorption in the various conditions of infantile malnutrition. According to Freund, even under abnormal conditions of nutrition, the fat absorption may remain perfectly normal, and he records instances in which with "soap stools" the fat absorption reached as high a value as 97 per cent. of the intake. On the other hand, Bahrdt,¹⁴ Birk,¹⁵ M. Chatruet,¹⁶ Hecht,¹⁷ and L. F. Meyer¹³ record in conditions of malnutrition with "soap stools" a fall in the fat absorption averaging about 80 per cent.

In all patients under our observation the fat absorption was considerably below normal (Table 3). The lowest percentage noted in Janes (Case 1) was 52.3 per cent.; the highest, 95.8 per cent., the average varying between 70 and 80 per cent. The greatest loss of fat was undoubtedly caused by diarrhea, and the most complete absorption can be explained by the addition of olive-oil to the diet of that period. The other fluctuations were conditioned by the quantity of the fat intake. On the day of the highest intake 78.6 per cent. was absorbed. In the other patients the absorption fluctuated within the same limits, namely between 70 and 85 per cent. The only exception with a considerably lower fat absorption is presented by Stocker (Case 3), in whom the lowest rate of absorption fell to 34.2 per cent. and the highest did not reach above 71.5

9. Keller: Arch. f. Kinderh., 1900, xxix, 1.

10. Freund: Jahrb. f. Kinderh., 1905, lxi, 36.

11. Birk: Jahrb. f. Kinderh., 1907, lxvi, 300.

12. Rothberg: Jahrb. f. Kinderh., 1907, lxvi, 69.

13. Meyer, L. F.: Jahrb. f. Kinderh., 1910, lxxi, 379.

14. Bahrdt: Jahrb. f. Kinderh., 1910, lxxi, 249.

15. Birk: Jahrb. f. Kinderh., 1907, lxvi, 69.

16. Chatruet, M.: Thèse de Paris, 1904.

17. Hecht: Jahrb. f. Kinderh., 1905, lxii, 613.

per cent. Again in this instance the low absorption was caused by increased peristalsis. On the other hand, the patient who showed the highest average fat absorption—Dolan (Case 7)—was receiving olive-oil. The beneficial effect of olive-oil on fat absorption had been noted already by Freund.¹⁸

According to his experiments the comparative degree of fat absorption on a diet containing no olive-oil, and one containing the oil (the total amount of fat intake being equal) varied as follows:

Cases	Diet	Per cent of Soap
A.	Meal	46.7
	Oil	7.9
	Malt	5.9
B.	Meal	57.0
	Oil	6.2
	Malt	5.0

In reviewing these observations on the fat absorption one is impressed by the fact that in all patients (with the exception of Dolan, Case 7), the loss of fat through the feces was not sufficient to cause in itself any perceptible deviation in the general nutrition.

C. Soap Content of the Feces

In health, according to Freund,¹⁹ the average proportion of insoluble soaps in feces is 18.3 per cent. of the total fat in the feces, the lowest figure being 4.9 per cent. and the highest 35.9 per cent. In conditions of malnutrition the average reaches 48.0 per cent., the lowest being 42.1 per cent. and the highest 57.0 per cent.

In the patients under our observation the soap content of the feces varied considerably. The percentage of soap in the stools of Janes (Case 1) was as a rule very high, 83.5 per cent. in one period, and gave an average of 46.3 per cent. for the thirteen periods. The low content of soap of 11.0 per cent. was conditioned by diarrhea and on two other occasions the low percentage of soap in the feces was caused by the addition to the diet of olive-oil.

Of the other patients a high percentage of soap in the feces was noted only in Dakak (Case 2), the average being 66.7 per cent. and, as can be seen from the following table, the soap content of the remaining patients did not exceed the normal value.

Patients	Per cent. of Soap in Feces	Patients	Per cent. of Soap in Feces
Janes	46.3	Franco	11.66
Dakak	66.7	Vogelin	13.8
Stocker	20.3	Dolan	34.
Guerin	20.9		

18. Freund: *Biochem. Ztschr.*, 1909, xvi, 453.

19. Freund: *Ergebn. d. inn. Med.*, 1909, iii, 163.

III. STOCKER

1	Mar. 17-18		8.61	7.87	.74	8.6	49.4	355.0	4.03		.57	1.00	.06	3.64	2.13	1.51
2	Mar. 19-21		7.74	5.15	2.59	33.5	58.6	148.6	3.21		.82	1.63	.34	3.67	2.05	1.62
3	Mar. 23-24		8.11	5.98	2.13	26.3	63.9	246.2	4.15		.67	2.19	.23	4.01	2.69	1.32
4	Mar. 26-27		7.06	5.88	1.18	16.8	56.7	222.4	4.08		.67	2.17	.15	4.01	2.65	1.36
5	Mar. 28		5.67	3.83	1.84	32.5	71.5	239.2	3.56			2.19	...	4.01	2.44	1.57
6	Mar. 29		10.18	10.18			34.2	279.4	4.65		.60	2.84	.11	4.01	3.18	.83
7	Mar. 31-Apr. 1..	1.39	1.05	1.05	.34	24.5	40.0	225.8	3.56		.67	.71	.13	3.57	1.81	1.76

IV. GUERIN

1	Apr. 13-16		2.04	1.41	.63	30.8	88.6	71.7	2.05		.24	3.77	.17	4.07	2.47	1.60
2	Apr. 18-25		2.85	1.85	1.00	35.1	87.3	68.0	2.04		.23	3.06	.33	4.12	2.16	1.96
3	Apr. 27-29		4.32	3.27	1.05	24.3	85.5	80.7	2.51		.38	2.57	.12	4.12	2.15	1.97
4	May 1-2		6.10	5.03	1.07	17.6	76.1	80.3	2.00		.23	3.82	.15	3.68	2.47	1.21

V. FRANCO

1	May 7-10		3.07	2.62	.45	14.7	80.5	141.4	2.77		.30	2.65	.13	3.64	2.30	1.34
2	May 22-27		3.23	2.84	.39	12.1	76.8	129.6	2.69		.17	5.24	.12	5.80	3.36	2.44
3	May 28-30		2.95	2.69	.24	8.2	77.3	95.2	2.73		.23	6.99	.12	6.31	4.12	2.19

VI. VOGELIN

1	May 13-15		4.42	3.81	.61	13.8	70.6	160.2	2.95		.32	1.78	.26	4.08	2.01	2.07
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VII. DOLAN

1	May 18-20		3.09	1.95	1.14	36.9	85.9	31.8	2.04		.26	2.54	.17	3.68	1.94	1.74
..	[May 18-19]		2.76	1.32	1.44	52.2	87.7	17.3					...			
..	[May 20]		3.76	3.20	.56	14.9	81.9	60.9					...			

The lowest percentage of soap was noted in Franco (Case 5), who at the time of the metabolism experiment was in a condition of convalescence. Vogelín (Case 6) also was in a condition of convalescence, gaining weight at the beginning of the experiment, although his condition became aggravated during the experiment. On the other hand, Dakak (Case 2) was apparently in a comparatively good condition, showing a gain in weight during the time of the metabolism experiment, and yet the percentage of soap in his feces was very high.

It must, however, be borne in mind that all other observations with the exception of the one on Janes (Case 1) were of comparatively short duration, and therefore are less instructive. But, even in the case of Janes, it is as yet difficult to determine the factors which control the soap formation. Comparing three periods, the fourth, fifth and sixth, which differ principally in the carbohydrate intake, one notes that the lowest percentage of soap formation coincides with the period of the highest carbohydrate intake. Also very instructive are the last three periods. They all differ principally in their fat intake. The highest content of soap in the feces coincides with the lowest fat intake. At first glance, the result seems very paradoxical. However, it is possible that the addition of olive-oil to the diet of the last two periods conditioned the improvement in the fat absorption and the fall in the ratio of soap formation.

Thus the analysis of the composition of the fat of the feces in infantile malnutrition leads to the conclusion that in this condition the fat absorption from the small intestines is diminished. The unabsorbed fat, fatty acid and alkaline soaps, therefore, reach the colon. There the fat, fatty acids and the alkaline soaps are transformed into insoluble calcium soaps.

D. Salt Content of the Feces

The abnormal soap formation may lead to a fundamental change in the character of the general composition of the feces, which in its turn may affect the general health and the growth of an infant. Thus, *a priori*, by the formation of calcium soaps, the insoluble phosphates may be transformed into soluble salts, and in this manner may suffer absorption. The theoretical considerations were corroborated by experiment. In healthy infants with a normal fat absorption, high fat intake remains without influence on the mineral composition of the feces. In chronic malnutrition the salt output through the feces is considerably raised by the fat of the diet. This was demonstrated by Steinitz,⁸ Freund,¹⁰ Rothberg,¹² Birk,¹¹ and L. F. Meyer.¹³ Experimentally the same effect of high fat intake was observed by Schlesinger¹⁹ on dogs after the removal of the pancreas. The loss of mineral bases after high fat intake may reach

19. Naunyn's Festschrift: Ztschr. f. klin. Med., 1904, lv, 214.

a degree sufficient to produce a negative salt balance, which alone may arrest further growth. This consideration perhaps more than anything else, led Czerny and Keller to the assumption that loss of mineral bases and the following acidosis are the prime factors in the pathogenesis of infantile malnutrition.

In the patients under our observation there was noted a considerable content of mineral bases of the feces. The fluctuations in the absolute quantities of mineral constituents removed by the feces did not follow the rise or fall in the percentage of the soap content of the feces. In Stocker (Case 3), with an average soap content of 20.3 per cent., the average ash content of the feces (weighed as sulphates) was 3.89 gm. per day, while in Janes (Case 1), with an average of 46.3 per cent., the daily output of ash (as sulphates) in the feces was 3.91 gm. per day. The absolute quantity of ash in the feces did not follow closely even the curve of the absolute quantities of soap removed through the feces; thus, in Janes (Case 1), with an average daily output of soap of below 2.0 gm., the ash output through the feces was 3.98 gm. per day, and in Dakak (Case 2) the daily output of soap was 2.7 gm. with a corresponding ash output of 2.78 gm. per day. Further, in Stocker (Case 3) a daily output of 1.41 gm. soap corresponded to 3.80 gm. of ash. This apparent paradoxical phenomenon is readily interpreted by the consideration of phosphoric acid output. A comparison of the phosphoric acid output through the feces of Janes, Dakak and Stocker (Cases 1, 2 and 3) reveals the fact that its value rises with the fall of the proportion of soap to ash. This observation is of great importance, for the reason that it demonstrates that in the chronic forms of infantile malnutrition the formation of fatty acids in the intestines does not reach the degree at which the ash content of the intestinal tract is insufficient to neutralize them. In such forms, the pathogenesis of the disease cannot be interpreted either in the light of insufficient fat absorption, or in the light of excessive loss of mineral bases, owing to the presence of unabsorbed fatty acids in the colon. The theory connecting the pathogenesis of infantile malnutrition with the phenomenon of the formation of soap stools is not applicable to conditions similar to those in our observations. Also Bahrdt²⁰ reached the conclusion that the quantity of fatty acids found in the patients under his observation was insufficient to neutralize all the mineral bases found in the feces. And yet in his observation the ratio of fatty acids to ash was much higher than in our patients.

MINERAL BALANCE AND ACIDOSIS

Thus the behavior of fat in the intestinal tract in chronic infantile malnutrition is insufficient to disturb markedly the salt output through

20. Bahrdt: *Jahrb. f. Kinderh.*, 1910, lxxi, 267.

the feces and, therefore, there is little reason to expect a pronounced disturbing effect of the fat intake on the general salt balance. The analysis of the tables (Table 3) shows that in all our patients the salt balance was positive. In Janes (Case 1), who was under observation for the longest period of time, the curve of the salt balance does not follow the one of fat intake, nor that of fat absorption, nor the curve of the soap content of the feces. Thus, the behavior of fat in the intestinal tract of our patient gave no cause for creating a want of mineral bases in the tissues, nor for creating the acidosis in the organism. This hypothesis is substantiated by the analysis of the curve of the ammonia-nitrogen elimination. Only in one patient, Stocker (Case 3) the ammonia output reached the value that indicates a condition of acidosis (average = 21.3 per cent.); in all other patients, as can be seen from the tabulation below, the average ammonia output is approximately normal.

AVERAGE AMMONIA NITROGEN OUTPUT

Patient	Per cent.	Patient	Per cent.
Janes	5.6	Franco	8.3
Dakak	9.1	Vogelin	11.2
Stocker	21.3	Dolan	4.4
Guerin	6.9		

In Janes (Case 1) the fluctuations in the ammonia output do coincide with the fluctuations of the fat intake, and thus they are in harmony with the observations of Czerny and Keller,²¹ Steinitz,²² on infants, and of Schittenhelm²³ on adults.

However, similar fluctuations under the influence of alteration in the diet may occur also in health. Thus, there is no evidence that the character of the intermediary fat combustion in our patients was disturbed in a manner to cause the condition of acidosis. The exception of Stocker (Case 3) was probably conditioned by an abnormally high intestinal fermentation.

SUMMARY OF THE ANALYSIS OF THE BEHAVIOR OF FAT IN THE PATIENTS UNDER OBSERVATION

This summary brings to light the following peculiarities in the effect produced by fat intake in the seven patients under our observation:

1. In all patients it undoubtedly produced an increased peristalsis of the small intestines. Whether this effect was produced by the fat independently, or whether the fat facilitated the similar action of the carbohydrates can for the present not be stated with a degree of certainty.

2. The increased peristalsis results in a fall of fat absorption and,

21. Czerny and Keller: *Jahrb. f. Kinderh.*, 1897, xliv, 25; 1897, xlv, 274.

22. Steinitz: *Monatsschr. f. Kinderh.*, 1902, i, 4, 225; *Centralbl. f. inn. Med.*, 1904, xxv, 81.

23. Schittenhelm: *Deutsch. Arch. f. klin. Med.*, 1903, lxxvii, 517.

3. In an abnormal composition of the feces, which expresses itself in a high content of insoluble soap.

However, the lack of fat absorption and the withdrawal of mineral bases by the unabsorbed fat did not reach a sufficient degree of intensity to be regarded as very important factors in causing the defective nutrition in our patients.

On the other hand, the fat of the food failed to produce the principal effect that it invariably causes in health. Namely, it failed to bring about in connection with the carbohydrate of the food the normal gain in weight in the patients, who did not suffer from any difficulty in nitrogen assimilation, and whose diet contained a sufficient amount of calories for normal growth.

In this peculiarity of fat metabolism undoubtedly is contained the principal difference of metabolism in infant malnutrition as compared with that in health. The primary cause of this abnormal form of metabolism is difficult to detect. It is conceivable that in the chronic forms of infantile malnutrition a certain vicious cycle is established. In the loss of adipose tissue caused by some disease, or by some temporary condition, the organism sustains a very grave damage of its heat regulating factors. Under these conditions a higher energy value is required for normal growth, while the average normal diet is insufficient to enable the emaciated organism to continue its growth at the normal rate. It is conceivable that the organism may grow at the expense not only of the food but also of the fat and of the carbohydrates of the reserve material within the tissues. This may last so long as the glycogen and fat from the tissues is not completely removed; after this, normal growth could be made possible only by an excessively high diet, rich in fat. Unfortunately in all of the patients under our observation, and in those recorded by other authors, there was noted a marked intolerance of the intestines for both fat and carbohydrates, which expressed itself in the appearance of increased intestinal peristalsis following a high intake of fat or carbohydrate. Therefore, in order to avoid diarrhea, both the carbohydrate and fat intake need to be limited. Under these conditions the moderate food intake can suffice for only one of the functions, either for growth or for storing up reserve material in the form of fat and carbohydrate. The tendency of the infantile organism for growth is more intense than that for storing up reserve material, and thus the organism continues to perform the function of growth under most uneconomical conditions. The continuous nitrogen retention without increase in body weight may be the expression of the condition in which growth was proceeding at the expense of the fat and carbohydrate depots. The analytical data on the composition of the tissues in infantile malnutrition furnished by

Steinitz and Weigert²⁴ may be regarded as supporting the view just expressed. The findings of these authors reveal a very low fat content of the tissues in this pathologic condition. The tissues of the child with infantile malnutrition contained only 2.31 per cent. fat, while according to Camerer, Jr.,²⁵ the normal tissues of infants of the first year contain 12.3 per cent.

It is, however, noteworthy that the deviation in the utilization of fat in infantile malnutrition is principally of a quantitative nature. The analysis of the curve representing the fluctuations in weight in Janes, indicates a certain correlation between rise in weight and increase in fat intake. It should be mentioned in this place that the possibility of nitrogen retention without a corresponding increase in the storing up of fat and carbohydrate has already been pointed out by Rubner,²⁶ who designated the condition by the term "*selectiver Ansatz*."

In conclusion we wish to remark that in course of the work the impression was gained that the addition of olive-oil to the usual diet in proportion of 1 to 2 per cent. of the volume of the total intake improved the utilization of the total fat. The feces returned to a composition approaching that of the normal feces, the salt balance also approached nearer the normal, and gain in weight increased in intensity. From the appended histories it can be seen that it had been employed in several cases with some promise of success.

CLINICAL HISTORIES

CASE 1.—Janes, 5 months old, was admitted to the Hospital Nov. 9, 1909. There was a history of continued loss in weight since his first month, occasional vomiting and several attacks of diarrhea during the summer. For one month before admission there was constipation and vomiting after every feeding. On admission the child was poorly nourished and had a greatly distended abdomen; weight, 4,176 grams. By November 13, the general condition had somewhat improved, digestion was better and the stools were normal.

The metabolism experiment was continued from November 17 till March 3, with interruptions, viz.: December 10 to 13; December 25 to 31; January 29 to February 14.

The weight at the beginning of the experiment was 4,134 grams. At first he appeared bright and happy. The best weight was on January 14, 4,672 grams. From January 21 to 31 there was fever, cough and a double otitis media. On this account the observations were interrupted.

On March 3, when the experiment ended, the weight was 4,261 grams, the stools thin and green, and the child did not look well. He was discharged March 7, weight 4,153 grams. Subsequent to discharge his condition improved and he gained in weight on a diet including much carbohydrate.

CASE 2.—Dakak, 7 months old, was admitted Jan. 22, 1910, with bronchopneumonia. From Sept. 14, 1909, to Jan. 20, 1910, the child had been in the hospital as a feeding case and was discharged in good condition. On readmission

24. Steinitz and Weigert: *Monatsschr. f. Kinderh.*, 1905-6, iv, 6, p. 301.

25. Camerer, Jr.: *Pfaundler-Schlossman, Handbuch der Kinderheilkunde*, 1. Aufl., Leipzig, 1906.

26. Rubner: *Das Problem der Lebensdauer*, München and Berlin, 1908, p. 110.

he was small and poorly nourished, with signs of moderate rachitis. By February 12, the symptoms of pneumonia had disappeared; he had gained in weight and looked well.

When the metabolism experiment was begun March 8, he weighed 4,179 grams. The stools were large and good. On March 15, the metabolism experiment was discontinued, as the child again developed a pneumonia. The weight was then 4,386 grams. He grew rapidly worse and died March 21.

CASE 3.—Stocker, 3½ months old, entered the Hospital March 2, 1910. There was a history of vomiting and diarrhea for three days before admission. He was moderately well nourished; not acutely ill; abdomen distended; stools thin and yellow; weight, 4,700 grams.

The metabolism experiment lasted from March 17 through April 2. The weight fell to 4,554 grams but his general condition appeared to be better at first. The experiment was stopped April 2 because the child became weak, with loss of appetite, and the weight had fallen to 4,322 grams.

His lowest weight was 4,204 grams on April 30. The albumin of two eggs was added to his daily food. Breast feeding was attempted but he refused to take the breast. By May 27, the child appeared greatly improved; the stools were normal; weight, 4,700 grams. On June 13, olive-oil, 2 grams three times a day, was added to his food. He continued to gain in weight and was discharged June 22 in good condition.

CASE 4.—Guerin, 3 months old, was admitted Dec. 11, 1909, with symptoms of an acute gastro-enteritis. He looked acutely ill. The stools were green and thin; the weight, 4,120 grams. He improved with the addition of breast feeding.

The metabolism experiment was begun April 13 and continued until May 3. Weight at the beginning was 4,320 grams and he gained to 4,451 grams. From April 26, olive-oil was given, at first 2 grams three times, later increased to four times a day. In spite of a cervical abscess and double otitis media the child continued to gain slowly and on June 14 weighed 4,643 grams, when he was discharged.

CASE 5.—Franco, 3 months old, was admitted to the Hospital April 19, 1910, with an acute bronchitis. He was small but fairly nourished. The stools were soft and contained some mucus and often soft lumps.

The metabolism experiment was started May 7 and continued to May 31 with an interruption from May 11 to 22.

At the beginning of the experiment the child was gaining and weighed 3,593 grams. On May 11 the weight was 3,704 grams and increased to 4,002 grams by May 22. During this time four grams of salt per diem were added to the food. This was increased to five grams, but he refused the food with this added quantity of salt. At the end of the experiment the weight was 4,074 grams. On June 4, olive-oil was added, 2 grams, increased to 4 grams three times a day. The child was discharged June 17, gaining in weight and in good condition.

CASE 6.—Vogelin, 4½ months old, was admitted to the Hospital April 13, 1910. For the month before admission the stools had been green and thin and there had been constant loss in weight. On examination the child was found to be greatly emaciated, with a distended abdomen and moderate degree of rachitis. Weight, 3,794 grams. He gained steadily in weight and strength and the stools became normal.

The metabolism experiment was begun May 13 and continued only to May 16. He was very restless, cried continuously, slept very little. There was some vomiting and the stools were soft and yellow. The weight was 4,115 grams at the beginning, but in the three days had dropped to 4,040 grams. The condition became gradually worse; the stools, thin and green; there was a low fever, and a general edema; and he died on May 29.

CASE 7.—Dolan, 2 months old, first entered the Hospital Oct. 19, 1909, with pyloric stenosis. His weight was 3,058 grams. He was readmitted for several short periods until March 8, when, at the age of 7 months, the mother consented

to leave him in the hospital. At this time the weight was 3,624 grams. He was extremely emaciated, and looked acutely ill. There had been daily lavage for some time and the vomiting had practically ceased. The condition then was one of marasmus. He gradually improved during the next two months.

On April 8, olive-oil was given, 2 grams three times a day. From 3,709 grams the weight increased gradually but steadily to 4,077 grams by May 5. May 18, weight was 4,139 grams.

The metabolism experiment was then begun but he was restless and fretful and in the three days of the experiment he lost from 4,139 to 4,083 grams. During the following week, however, he gained 75 grams. On June 6, olive-oil was increased to four grams three times daily. The stools were good and the child continued to gain, weighing 4,494 grams when discharged June 21. Four months later he was still gaining.

A CONTRIBUTION TO OUR KNOWLEDGE OF THE
ETIOLOGY AND NATURE OF HARD
CURDS IN INFANTS' STOOLS *

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The curds that occur in the stools of infants, especially of those fed on cow's-milk, have been the subject of much discussion among pediatricians. A great deal of importance attaches to the solution of the problem of their etiology and nature, because their presence in the stools has always been considered an evidence of an overstepping of the infant's tolerance for the particular food element from which the curds were thought to be derived. The pendulum has swung from the first natural interpretation that they were undigested particles of curdled milk, therefore chiefly protein in origin, to the opposite extreme, if we are to accept the teaching of nearly all the foremost German pediatricians, that the casein takes no part in their formation. From observations that we have made in our clinic at Northwestern University Medical School, and from some experiments that I have made in the past year, I believe we are justified in stating that one extreme is nearly as far from the truth as the other.

The source of confusion lies in two places: (1) There is a lack of sharp definition of different kinds of curds; (2) German clinicians, as I hope to demonstrate, use a food that differs vitally in just this tendency to the formation of curds of a certain kind, from that which we, in this country, use as a routine. For this reason, which I will elaborate, I believe that certain curds do not occur in the experience of German pediatricians as they do in ours and that, therefore, the controversy concerning them runs in parallel rather than opposing lines.

The curds of infants' stools are distinctly of at least two kinds that differ essentially in morphology, etiology and composition:

1. The small, soft, friable, yellowish or whitish or greenish curd—the common curd of milk indigestion. This requires no further description. It has been removed from the field of discussion, almost universal consent in the last few years having given it predominatingly a fat origin. This curd occurs both when breast-milk and cow's-milk are fed.

2. The large, hard, tough curd. This curd bears no morphologic resemblance to the former, nor does it occur under similar conditions.

*Read before the Chicago Pediatric Society, Feb. 21, 1911.

It varies in size from a mere shred or that of the head of a pin to that of a lima bean or even that of the distal phalanx of a thumb. It is commonly the size of an ordinary white bean and is generally bean-shaped, or oblong or rounded, though often, especially if very large, it is quite irregular. It is always hard and usually can be broken or crushed only with considerable force. It is of about the consistency and appearance of hard American cheese. It can be picked out of a stool with a pin or a stick, without being injured, as definitely as can a bean. So strongly is its resemblance to a soaked bean stripped of its coat that at Northwestern we commonly call them "beans," for short. On one occasion a Mr. McGuire reported at the diet kitchen that "Elizabeth wasn't doing well at all, but what could you expect when the woman was feeding it beans," and he exhibited a very convincing diaper. These curds can be washed in water with great force, shaken in water in a bottle, for example, without any tendency to disintegration, and always sink rapidly to the bottom. When separated and dried they form dry, hard, shriveled, semi-translucent masses that resemble pieces of gelatin, or of horn. Finally they crumble to a coarse crystalline powder when touched, or even crumble spontaneously.

These hard curds are either white or dough-colored, or even light greenish; or else a pale, brownish-yellow or amber color. The former are softer and more nearly friable, usually more rounded than the latter and are accompanied by a greater degree of indigestion, as shown by the occurrence of mucus and an increased number of bowel movements. The yellowish or amber-colored curds are always very hard, and can be bent without breaking. They are often accompanied by indigestion, but about as frequently occur in an otherwise nearly normal movement. The two varieties of hard curds rarely, if ever, occur together, but one kind may merge into or follow the other with the baby on an identical food, depending on whether the indigestion improves or gets worse. For this reason, and because of their striking points of resemblance, there can be no doubt that they have a common origin.

The present discussion deals wholly with these hard curds. They are distinctly rarer than the soft curds when certain kinds of food mixtures are used, distinctly more frequent when others are used, and, again, never occur when certain conditions are complied with. They do not occur in breast feeding.

The present state of our knowledge of these hard curds has recently been focused in a rather heated discussion between Fritz Talbot of Boston on the one hand, and Ludwig Meyer of Berlin, and Jerome Leopold of New York, on the other. Talbot has published a series of articles on the subject of hard curds and presents an array of evidence that has convinced him that they are of casein origin, in contradistinction to the

small, soft curds that he, too, has found to be derived chiefly from the fat. Meyer and Leopold categorically and with considerable warmth deny all of Talbot's assertions. They speak constantly of "casein masses," not, however, in the sense in which Talbot uses the term, i. e., to designate hard curds, but as a general term synonymous with curds. When Talbot in a later paper takes them to task for not clearly differentiating between small, soft and large, hard curds they emphatically refute this criticism. A careful reading of their papers in the light of my own experience convinces me, nevertheless, that Meyer and Leopold are not using the term "casein masses" as synonymous with hard curd, even when especially asserting that they do. The only possible explanation for such antagonistic opinions about so decided a phenomenon can be found in the fact that Meyer and Leopold are not practically familiar with the hard curd that Talbot, Southworth, and other American observers have described so unmistakably.

The matter assumes greater importance when we realize that in this respect Meyer and Leopold represent all of the leading German authorities, Heubner, Czerny, Finkelstein, etc.

The explanation for this lack of familiarity lies, of course, not in a lack of observation; no one would ever accuse a German pediatrician of all others, of that; but in the simple fact that these curds do not occur in their experiences, while they are common in ours, for reasons that I will elaborate presently.

The arguments that Talbot presents are, to my mind, alone convincing that these hard curds are derived from casein. The evidence that I will present will, I believe, help to clear the matter because it will enable Meyer and Leopold to make these curds experimentally, so that they too can see and study them.

That the hard curd is of casein origin seems probable from its very appearance and consistency. It is, *a priori*, almost unthinkable that it is a fat, or a salt, or a bacterial, or an intestinal secretion derivative.

Further, when fat-free milk is coagulated with rennin and then broken up, the large curds, if separated, continue to contract and express whey. They then shrivel up into hard semi-translucent, horn-like masses and finally crumble in the fingers to a coarse powder, all of which bears a striking resemblance to what takes place in these hard curds when allowed to dry in the same manner. The curd of whole milk does this less readily and remains less dry, as if dipped in butter.

Furthermore, as Talbot has shown, and as I have been able to confirm, when a mass of curdled milk is left four to six hours in 10 per cent. formaldehyde solution it becomes as hard as a billiard ball; in fact, Talbot tells us that this principle is employed in the manufacture of

billiard balls. An identical result is obtained when a hard curd is thus treated.

Microscopically, too, Talbot has shown that there is an identical appearance in hard curds and in curds made artificially by coagulating milk with rennet, and digesting the resulting curds for one hour at 98.6 F. with pepsin and 0.2 per cent. hydrochloric acid, and then, after washing, further digesting them for one and one-half hours with a fresh 25 per cent. alcoholic extract of pig's pancreas in 5 per cent. of carbonate of soda. In both natural and artificial curds there is found a white, shining, translucent network in which numbers of neutral fat drops are entangled, that evidently could not be reached by the digestive juices because of their casein envelopes. Small curds, on the other hand, as one would expect, show the fat almost entirely in the form of fatty acids and soaps.

Talbot furthermore was able to demonstrate that "curds made and digested artificially give exactly the same physical and chemical composition as natural curds." He was "able to dissolve and precipitate these tough curds, in the same way as casein, by weak alkaline and acid solutions. This precipitate was obtained in as pure a state as possible and found to contain nearly the same percentage of nitrogen as Hammerstein's pure casein."

In spite of this evidence Meyer and Leopold maintain that casein takes no part in the formation of these curds; that the nitrogen is derived from some other source, possibly, as Langstein suggests, from the intestinal secretions. Talbot then brought out a proof that these hard curds do contain casein by showing that they give a specific biologic reaction. He prepared a specific anti-cow casein serum by injecting rabbits with cow casein. With lactalbumin and human casein he obtained no precipitate with this serum, but with cow casein and with the hard curd the reaction was positive. Normal stools not containing these hard curds gave no such reaction.

That these curds are not derived from the fat of the food is demonstrated by the fact that they occur just as frequently with the use of fat-free milk as with whole milk, or cream; in fact, in my experience, for reasons that will appear later, they have occurred predominately with fat-free milk. In all of the experiments that I will present certified, centrifuged, fat-free milk was used.

When Czerny's chapter on *Milchnaehrschaden* first appeared we were convinced, in the light of former experiences, of the truth of its teachings concerning curds and protein digestion and increasing experience more and more confirmed the view that there was no pathologic clinical picture which could be recognized as due to casein. Prior to this time we had been followers at the clinic of the so-called percentage method of feeding.

We fed high fats and low proteins and commonly "split" the latter to get away from the "casein" curds that constantly followed us. Babies were fed almost exclusively on cream and milk and whey mixtures and while we saw innumerable small fat curds the hard curd was so rare that I, personally, had never thought of it as a distinct clinical entity. Convinced that the protein was harmless we fed it boldly in fat-free milk in almost any amount and in almost any condition and were more and more impressed with its harmlessness. The curds that we had seen so frequently formerly never appeared so long as we used fat-free milk alone.

Only one thing stood in the way of our happiness and that was the appearance in certain cases, for the first time in our experience, of an appreciable number of hard, bean-like bodies in otherwise fairly normal, fat-free milk bowel movements. After a time we noticed that these hard curds came fairly regularly when we exceeded a certain amount of fat-free milk. Personally, I came to expect them in the less tolerant cases whenever I exceeded 2 ounces of fat-free milk to the pound of baby and I gradually thought of this as almost the limit of tolerance for many cases. When the limit of tolerance was exceeded there often appeared other evidences of indigestion, the bowel movements became paler and softer, contained mucus and became noticeably more frequent. Up to this time we used raw milk practically exclusively. To counteract the diarrhea, we resorted to the time-honored expedient of boiling the milk, and found almost without exception that the digestion improved, and that *without any exception the hard curds disappeared in a day or two without otherwise altering the food*. Since that time we have nearly always boiled the milk in these less tolerant cases, always to begin with, and now again we never see the hard curd in our own experience at the clinic except as a result of a mistake in judgment. In all of our experience *we have never seen a hard curd unless a considerable amount of raw milk casein was given and we have never seen them persist or occur when boiled milk, no matter in what amount, was given*.

In a case of decomposition (Finkelstein) in which I had been feeding the patient boiled fat-free milk for some time, hard curds suddenly appeared in the stools for the first time. I expressed my regret to the mother that she had not carried out my order to boil the milk. She maintained that she had boiled it and I stated positively that the baby had had raw milk. She then suddenly remembered that in her long-extended anxiety and sleeplessness she had become absent-minded and had wholly forgotten to boil the milk on the previous day. The curds never again appeared.

To do away utterly with the possible element of coincidence I decided to make and unmake hard curds at will, in babies, by the simple expedient of using raw and boiled milk alternately. The result was as precise as

a chemical reaction in a test-tube, in each of four babies, i. e., in every baby in which it was tried.

These four babies represented different pathologic conditions and different ages. None of them was, of course, critically ill at the time of the tests themselves. They were watched with the utmost care and none of them became ill during the tests except for a slight temporary diarrhea in some of the cases. Inasmuch as the fat was eliminated and the sugar low in the foods, I felt that there was no possible danger to the babies from the serious disturbances, such as an intoxication. The remedy was always immediately at hand if a baby became only slightly ill, and inasmuch as the remedy consisted in boiling the milk the course of the experiment was not disturbed.

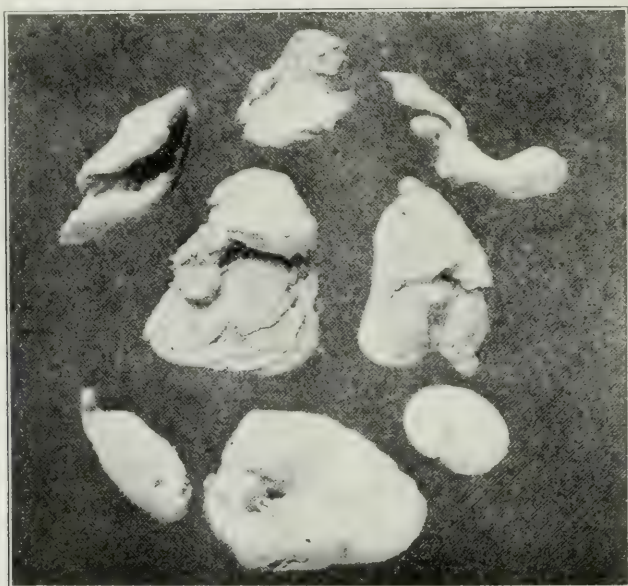


Fig. 1.—Casein curds, actual size (taken from Talbot). The curd in the lower right hand corner shows the usual size and appearance of the commonest bean-shaped hard curd. The larger ones show the indentations that appear, as though portions of the curds had been digested out. These curds are so evidently identical with those described in the text, especially to those who have seen them often, that no apology is necessary for utilizing this excellent photograph.

In every case certified, centrifuged fat-free milk was the only milk used. The reason for this was fourfold: (1) It was the food that seemed indicated therapeutically; (2) it eliminated largely the fat in determining the origin of the hard curds; (3) hard curds are made more easily with fat-free than with whole milk; (4) and most important, it eliminated practically all source of danger to the baby. Whole milk in a

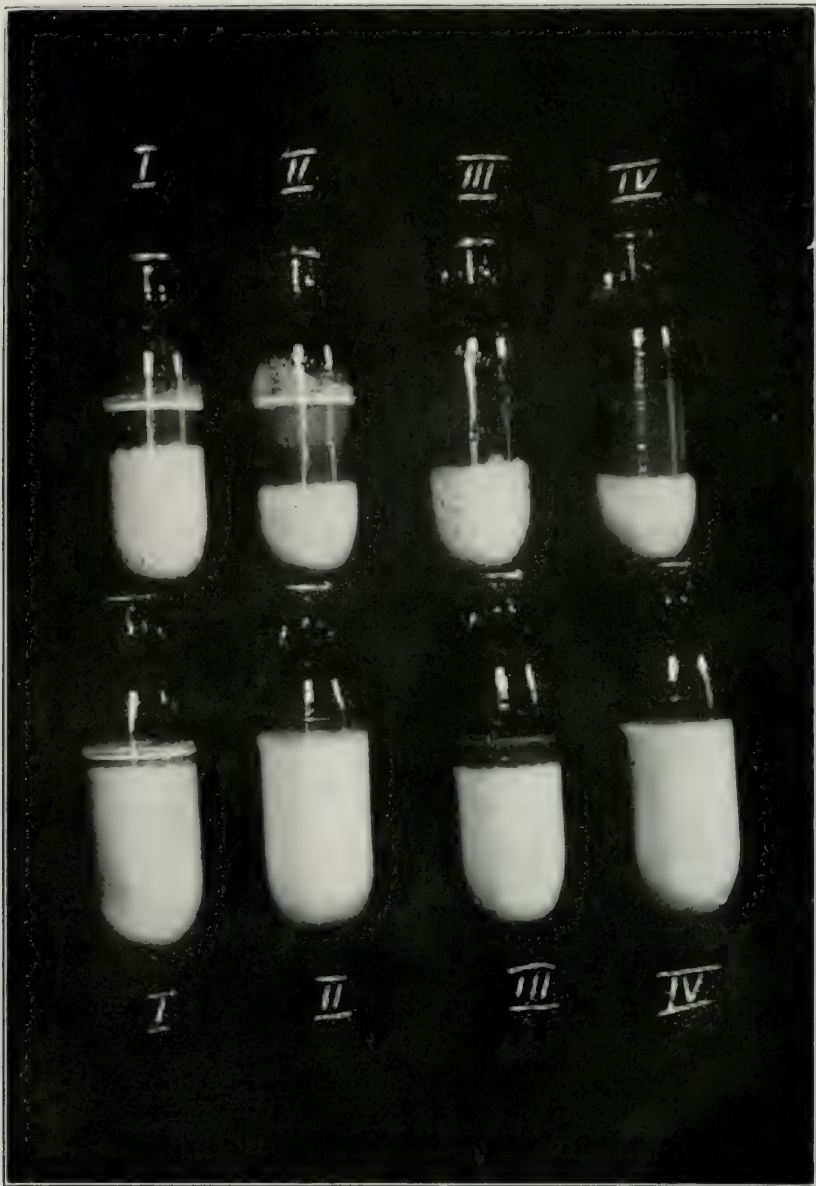


Fig. 2.—Photograph showing the effect on milk coagulation with rennin of boiling and of dilution with water. Each of the above bottles of milk was treated with the same amount of rennin (chymogen) at a temperature of 105 F. for thirty minutes, then shaken, cooled, and allowed to stand for forty hours. The upper row of bottles contained raw milk, the lower row milk that had been boiled five minutes. Bottles I contained undiluted whole milk; bottles II, equal parts of whole milk and water; bottles III, undiluted fat-free milk; bottles IV, equal parts of fat-free milk and water. Note the greater separation of whey in all the upper (raw) bottles and the coarseness of the coagulum, particularly in the undiluted bottles I and III, and especially in the undiluted, fat-free milk bottle (III). In the lower row is shown the very imperfect separation of whey, and the fineness of the coagulum when the milk is boiled, and especially when also diluted, as in bottles II and IV.

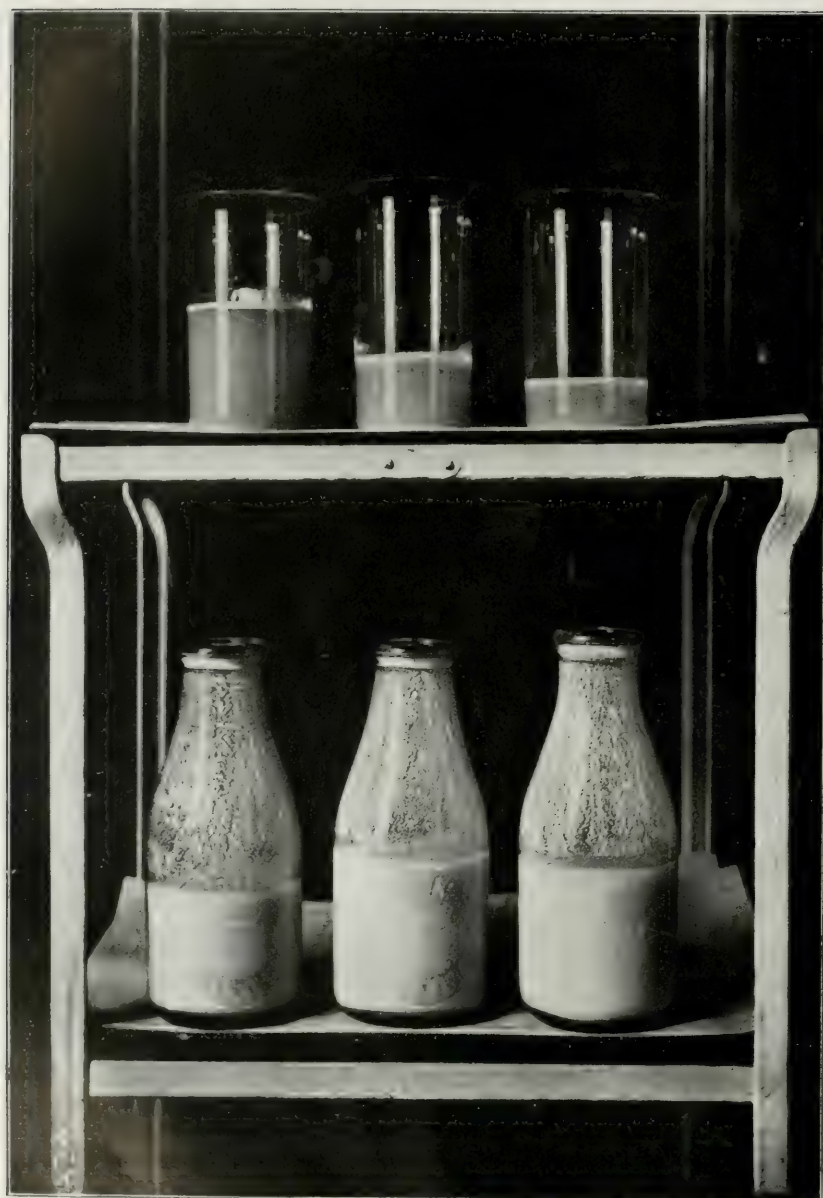


Fig. 3. Eiweissmilch (Finkelstein) prepared with raw and boiled milk. The three quart milk bottles, from left to right, represent the amount of eiweissmilch made according to Finkelstein's directions from one pint each of raw milk, milk just brought to a boil, and milk boiled five minutes, respectively. Above each bottle is shown the amount of whey extracted from that pint of milk. With raw milk the whey was about double, and the curd about one-half (by weight) that of the boiled milk. The difference in fineness of the curd is not evident in the photograph.

sufficient amount to give an abundance of hard curds would probably have produced many small fat-curds, or a soap stool, or would have been a serious menace to an atrophic infant. The fact that none of the babies suffered in any way beyond a slight temporary indigestion demonstrates again the insignificance of the rôle played by the proteins in nutritional disturbances as compared with the fat or the sugar. When the milk was boiled this was done in a single boiler for two to five minutes. In every instance the food was begun at 4 p. m., the stools inspected the next forenoon, and a day corresponded to a calendar day.

It will be necessary to give these cases in sufficient detail to show the conclusiveness of the evidence.

CASE REPORTS

CASE 1.—Baby B., aged 4 months, weight 10 pounds 5 ounces; nursed two months, then fed cow's-milk whenever it cried, had been sick ever since; had five to six dyspeptic stools a day. The baby had a typical, profound intoxication (Finkelstein), with low fever.

The patient entered Wesley Hospital Oct. 7, 1910, and was put on *boiled* fat-free cow's-milk, 15 ounces, barley water, 15 ounces, for three days. In the next two weeks the food was gradually increased to fat-free cow's-milk (*boiled*), 22 ounces, and human milk, 10 ounces a day. In the first week there were five to nine dyspeptic stools a day and the child was generally edematous, with dry, hard, leathery skin and tissues. During the second week these symptoms all disappeared, the look of intoxication was no longer present, the digestion became normal; the baby had one or two stools a day and gained 2 ounces. Up to this time the cow's-milk was always boiled and no curds had appeared.

October 20. *The milk was now ordered raw* and consisted of fat-free cow's-milk, 22 ounces, human milk, 5 ounces, barley water, 13 ounces, flour-ball, $\frac{3}{4}$ ounce.

October 21. One normal stool, no curds.

October 22. Two stools, one at 1 a. m. contained one hard curd and a later stool had three large, white hard curds the size of small lima beans. The first curd appeared thirty-three hours after food was given raw.

October 23. Four stools containing hard curds.

October 24. Seven stools each containing large, hard, whitish curds varying in size from a small pea to a large marble, or filbert, and forming often apparently more than one-half of the bulk of the movement. The rest of the stool was liquid and greenish.

Because curds often appear more freely when undiluted milk is given, to eliminate further the additional carbohydrate, and for more accurate experimental purposes, the baby was now put on 30 ounces of raw undiluted fat free milk.

October 25. Five stools of same consistency, each containing large, white, hard curds. The same food was now given boiled five minutes.

October 26. Five loose, somewhat greenish stools; 2 a. m. stool had a few yellow or amber-colored curds the size of a split pea. Baby looked better.

October 27. Four stools. Two contained hard curds, one a few small yellow ones; the other has several larger and a number of smaller yellow curds. No more curds after the 12:30 stool, i. e., forty-four hours after the milk was boiled.

The baby was kept on this same fat-free milk, 30 ounces, for six days. It had four or five thin but greatly improved stools a day, in none of which were there any curds. Baby in good condition.

November 2. Same food, 30 ounces fat free milk again ordered raw.

November 3. Four stools; fourteen hours after beginning raw milk one stool contained many typical, large, whitish curds the size of a lima bean.

November 4. Four stools. One contained one very large, hard curd; the rest all had several small, yellow, hard curds.

November 5, 6 and 7. During these three days the baby had four and five stools a day, some of which each day contained small and large yellow hard curds. The food was then changed to whole cow's milk, 12 ounces, barley water, 18 ounces, boiled five minutes.

November 8. Four stools. Two large yellow curds in the morning stool, none after that. During the next four days $\frac{1}{2}$ ounce of a malt food was gradually added to the food. The stools became normal, rather constipated, with no curds of any kind at any time. The baby left the hospital five days later in excellent condition, having lost only 11 ounces in spite of the severe intoxication and edema at the start.

In this baby we felt in advance, on account of its age and recent dyspepsia, that we had a favorable case for large curd formation. The large, white curds of the first trial were an evidence of a severer reaction; the smaller, yellow, harder curds of the second trial showed that the child's ability to handle an excessive amount of raw fat-free milk had improved greatly. Especial interest attaches to the fact that in spite of the sudden addition of a considerable amount of fat in the 12 ounces of whole milk, and of carbohydrate in the form of barley water and malt food, no more curds appeared when the milk was boiled five minutes.

CASE 2.—Baby W., entered Wesley Hospital Nov. 20, 1910. Age $5\frac{1}{2}$ months, weight $7\frac{1}{2}$ pounds; had lost 6 pounds; breast-fed one and one-half months; then a fine fat baby. The infant was then put on various foods, finally on pasteurized cow's-milk. It was always extremely constipated, so that it had marked prolapse of the rectum.

Diagnosis, simple malnutrition. On account of the good digestion and marked constipation the baby seemed especially favorable, because it would not be likely to be acutely upset.

From Nov. 30, 1910, to Jan. 20, 1911, the infant was given various whole-milk, fat-free-milk and human-milk mixtures with carbohydrate additions. The cow's-milk was always boiled. The child was so constipated that commonly $\frac{1}{2}$ ounce of milk of magnesia was added to the food. *For one month the baby was now kept on the same food, 30 ounces of fat-free milk, daily.*

January 20. Put on fat-free milk, 30 ounces, boiled five minutes.

January 21. Two stools. No curds.

January 22. One stool, constipated, no curds.

January 23. Two normal fat-free milk stools. No curds. Milk ordered raw.

January 24. One stool, dry and constipated. No curds.

January 25. One lighter, softer, stool containing many small yellowish bean-like curds, about thirty-two hours after raw milk was started.

January 26. Two stools. Each had large and small, hard, yellow curds, larger than on the previous day.

January 27. Two stools. First had six or seven small, yellow curds; second had more hard yellow curds than any previous stool.

January 28. No stool. Milk boiled two minutes.

January 29. Two stools. Three hard yellow curds. None after twenty-four hours of boiled milk.

January 30. One stool. Very constipated. Stool like marbles. No curds.

January 31. Two stools. No curds. Same food again ordered raw.

February 1. One stool. Seven large and small yellow curds within fourteen hours of giving raw milk.

February 2. One stool softer and paler; seven yellow curds of medium size.

February 3. One stool; seven yellow curds.

February 4. One stool; eleven yellow curds, some quite large. Sodium citrate, gr. xxx, added to the same raw milk.

February 5. One stool; same number and size of curds.

February 6. One stool; same color and consistency. One large and two small yellow curds.

February 7. One stool, same as before, contained six yellow curds. Sodium citrate, gr. lx, added to same milk raw.

February 8. Two stools. First, at 10 a. m., had seven or eight very small, yellow curds; second, in the afternoon, contained no curds. Sodium citrate reduced to 30 grains.

February 9. One stool; one large and several smaller hard yellow curds. Sodium citrate again increased to 60 grains.

February 10. One stool; six very small, yellow curds.

February 11. One stool; no curds. Curds ceased as before in twenty-four hours when sodium citrate was increased from 30 to 60 grains. Sodium citrate omitted. Milk still given raw.

February 12. One stool; first part hard and contained no curds.

Last part of same stool was softer and contained two yellow curds.

February 13. Two stools; each contained several hard, yellow curds, one very large.

February 14. One stool; contained a number of very large, hard, yellow curds and several smaller ones. Milk ordered boiled two minutes.

February 15. One stool; two large and three small yellow curds.

February 16. One stool. No curds. Same milk ordered raw.

February 17. Two stools. One early a. m. had no curds. One at 7 p. m. contained twenty to thirty large and small hard, yellow curds.

February 18. One stool liquid, pale yellow. About twenty medium and small, paler yellow, nearly whitish, softer, hard curds. Milk at once given boiled two minutes, because of the condition of the movements.

February 19. Two stools. One at 2 p. m. had several small, harder, yellow curds. Second at 9 p. m. contained one very small curd the size of two pinheads and several shreds.

February 20. No stool.

February 21. Two stools, no curds; baby in good condition.

A special point of interest in this case is the fact that when enough sodium citrate was given its action in stopping the formation of curds was identical with that of boiling the milk.

CASE 3.—Baby S, aged 23 months; weight 14 pounds; undersized child with typical *Milchmaerschaeden* (Czerny); typical soap stools. In this case I had considerable misgiving as to our ability to produce hard curds at all, on account of the child's age and good digestion and I felt that large amounts of undiluted fat-free milk would have to be given to reach the desired result.

October 17. The child entered Wesley Hospital and was given water until the following morning.

October 18. The following food was ordered: Fat-free milk, boiled, 18 ounces, barley water, 18 ounces, flour-ball, $\frac{1}{2}$ ounce.

October 19 and 20. Child normal in every way. Food increased to fat-free milk (raw), 28 ounces, barley water, 8 ounces, flour-ball, $\frac{1}{2}$ ounce.

October 21 and 22. Bowels rather constipated; no curds; food increased to fat-free milk (raw), 32 ounces, barley water, 10 ounces, flour-ball, $\frac{1}{2}$ ounce.

October 23 and 24. No change of any kind. Food now limited to fat-free milk 48 ounces raw.

October 27. Sixty hours later one or two stools contained yellow, hard curds.

October 28. Three stools with several large bean-like, yellow curds in one of them.

The child was now put on whole milk, raw, 10 ounces, fat-free milk, raw, 23 ounces, barley water, 15 ounces, flour-ball, 1 ounce, thus adding fat, increasing

the carbohydrates and lowering the protein and salts only. For the next eight days the child had daily from one to two movements that were well digested and contained no curds. The food during this time was gradually increased to whole milk (raw), 20 ounces, fat-free milk (raw), 13 ounces, barley water 15 ounces, flour-ball, 1½ ounces. This, together with some additional soft food, brought on a slight diarrhea, with three to five stools daily on November 6, 7 and 8, and on the 9th there again appeared several yellow, hard curds. The same food was now boiled; the digestion quickly became normal in every way and no more curds were found. The child gained 2 pounds during the four weeks in the hospital. At no time were the curds abundant, but they were morphologically identical with those of the previous baby and were always, as one might expect, of the hard, yellow type that accompanies less severe disturbances.

CASE 4.—Baby K., 6 months old, weight 11 pounds; very pale; simple malnutrition; no stool for first forty-eight hours in the hospital. The infant entered Wesley Hospital Oct. 16, 1910, and was given fat-free milk boiled 5 minutes, 15 ounces, barley water, 15 ounces, flour-ball, ½ ounce.

October 17, 18 and 19. One movement daily, normal in every way.

October 19. Same food ordered given raw.

October 20. Stools normal with enema. Fat-free milk raw increased to 22 ounces; food otherwise the same.

October 21. One normal stool.

October 22. Four stools. Nearly all of them contained a number of yellow, hard curds. Food increased to fat-free milk (raw), 24 ounces, barley water, 12 ounces, flour-ball, ½ ounce.

October 23. Three stools, containing some curds as before.

October 24. Four stools, no curds.

October 25. Five stools. Only one of these contained small yellow curds.

October 26. Three stools, with a few small yellow curds. As in the previous cases the food was now changed to undiluted raw fat-free milk—in this case 36 ounces.

October 27. Six stools. Last one contained several yellow curds.

October 28. Five stools. One contained several small bean-like yellow curds.

October 29. Three stools. First one contained several large yellow curds.

October 30 and November 1 and 2. Five, two and five stools, respectively. No curds.

November 2. Five stools. A few yellow curds in one of them. Milk now ordered boiled.

November 3. Five stools. One curd in one of them.

November 4. Five stools. No curds except a few the size of a pin head in one of them. No more curds after that, even when put on whole milk (boiled), 12 ounces, barley water, 18 ounces.

The infant left the hospital November 21, in good condition. In this case the baby was older and heavier than baby B, had no digestive disturbance to begin with, and its ability to handle a large amount of raw, fat-free milk was much greater, as shown by the fact that the curds were never abundant, were always of the hard, yellow type, and even showed a tendency to disappear while on raw milk. A larger amount of raw milk would doubtless have caused more curds to appear, but the frequency of the stools did not warrant such a procedure.

Having now demonstrated that in all of the cases in which it has been tried (and one would hardly be justified in trying it on more cases, even though the experiment is harmless), hard curds have been made to appear when a sufficient amount of fat-free milk was given raw, and made to disappear, without an exception, when the milk was boiled, I believe one is justified in making a general application of this fact, especially so when

combined with our former extensive collective experience at Northwestern, in which the same condition was always found.

That whole milk will produce the same hard curds will be doubted only by one who has never seen identical hard curds when whole milk was fed raw. That they occur only infrequently when whole milk or cream mixtures are used is easily explained by the fact that nearly always the fat or the added carbohydrate will produce serious disturbances long before so small an amount of casein, if we may accept this as the origin of hard curds, will produce any changes. Then too, on account of its greater food value, whole milk is used in less amount than fat-free milk would be for the same baby. For reasons which will appear later, it is very probable that hard curds are formed more readily with fat-free milk than with whole milk or cream. For curds to appear in fairly normal babies the raw milk must be excessive; the more nearly undiluted the more likely are curds to appear; or the baby must be in a condition that cannot yet be defined sharply in which it cannot handle even a small amount of raw milk. Thus in the two more delicate cases, Baby B. and Baby K., curds began to appear when 2 ounces of raw, fat-free milk to the pound of baby were given. In Baby W., which seemed to have a better digestive capacity in every way, curds appeared with 3 ounces, and in the older child, Baby S., with a practically normal digestion, even $3\frac{1}{2}$ were required.

An explanation of the phenomena I have described does not seem hard to find. In the last year I have made a large number of experiments to determine the difference, *in vitro*, of raw and boiled milk in the presence of rennin. This difference, in a general way, is familiar to all of us, and yet we have not been sufficiently impressed with it, nor have we made such practical applications as readily suggest themselves. I will give in a general way only those features of these experiments that have bearing on the main point here at issue.

Undiluted raw milk when treated with rennin at body temperature will thicken in a few minutes, will then form a firm, hard jelly that will hardly fall from the inverted beaker. This clot then contracts to a smaller bulk while whey is separated from it. If broken up with a spoon at the end of fifteen to thirty minutes there will be a definite separation of large cheesy curds, and a more or less clear whey. If the curds are separated from the whey and set aside it will be found that they naturally keep on contracting with the further expression of whey. They soon become as hard as the white of a hard-boiled egg. If allowed to dry longer they finally resemble pieces of hard gelatin or horn, very strikingly like the hard curd dried in a similar manner.

If, now, undiluted cow's milk that has been boiled for five minutes is treated in the same manner, very significant differences are soon appar-

ent. Coagulation is not only greatly delayed, but even at the end of half an hour at a temperature of 100 to 105 F. the curd is very soft and friable, about like a good custard. When this is now broken up as before with a spoon there is no marked separation of hard curd and whey, but the whole mixture still looks like a thick, fluid milk, about the consistency of buttermilk. On drinking it one notices only a slight thickening of the milk; distinct curds are not evident.

If the experiment is repeated with diluted raw milk, say equal parts of raw milk and water, a further striking change is noted. Coagulation is much retarded and the resulting curd is less firm and tough. Nevertheless, when the coagulum is beaten up the mixture will consist, as before, of firm separated curds, less tough, however, than when undiluted milk is used, and whey. If an identical dilution of milk and water is boiled for five minutes and then treated with rennin, there is almost no perceptible coagulation and only the slightest thickening, even at the end of thirty minutes.

With other dilutions, and with different lengths of time of boiling, the following general principle is established: The more milk is boiled, or the more it is diluted, the slower the coagulation and the less firm the coagulum. Or, in other words, the rapidity of formation and the firmness of the coagulum vary directly with the amount of casein, and inversely with the length of time of boiling. Milk diluted more than one-half and boiled ten or fifteen minutes is practically non-coagulable with rennin in such amounts as was used in these experiments. Pasteurized milk acts in this respect like raw milk.

When fat-free milk is used in these experiments instead of whole milk the resulting curd is tougher (almost leathery when the milk is raw and undiluted) than with whole milk. When dried this same thing is equally true; the resulting curd from raw, undiluted, fat-free milk is nearly white and becomes hard as bone, long before the yellower, softer, more friable, greasy, whole milk curd has become nearly so hard. The latter is doubtless due to the fat held in the casein. Ultimately when continued drying takes place these curds will crumble between the fingers into a coarse crystalline powder just as do the hard curds from the stools. In both natural and artificially made hard curds Talbot found further that the fat content varied directly with the amount of the fat in the food and in the milk from which the artificial curds are made, respectively.

In vitro, then, if we thought of the contents as food, raw milk and especially raw fat-free milk would be considered a mixture of a solid and a liquid food, and boiled milk would be a liquid food, very similar in this respect to an infant's natural food.

But we are told by Czerny that deductions made from what goes on in the beaker cannot be applied to conditions in the stomach. He states, furthermore, that if the milk is constantly stirred or agitated in a beaker firm coagulation cannot take place.

Simply to confirm this finding I did the following experiment and was astonished at the result. In four beakers containing 4 ounces each of undiluted, whole, raw milk, undiluted whole milk boiled five minutes, undiluted fat-free milk raw, and undiluted fat-free milk boiled five minutes, I placed the same amount of chymogen (about $7\frac{1}{2}$ grains) and kept them at a temperature of 100 to 105 F. for fifteen minutes. Duplicates of each of these were made and while the one set was allowed to coagulate undisturbed, the other set was constantly and vigorously stirred with a spoon. At the end of fifteen minutes the contents of each of the eight beakers was stirred vigorously.

In the case of the undiluted, raw, fat-free milk that was stirred constantly the separation of curd and whey was most complete and the curds were large, from a pea to a marble in size, and were more tough and leathery or rubbery than I had ever seen them before, while in the undiluted, fat-free milk not stirred the separation was less complete, and the curds smaller and much more easily divisible. In the raw whole milk the difference was even more striking, possibly due to the fact that some one else stirred this beaker and may have used more of a rotary than a criss-cross motion. In the unstirred beaker the separation was fairly complete, but the whey was milkier, while the curd was quite firm but still easily divided into smaller curds on stirring. In the beaker that was stirred constantly the whey was very milky and practically all of the curd was in one tough ball nearly the size of a walnut.

In the boiled, undiluted, whole milk beaker that was unstirred, the mixture after stirring at the end of fifteen minutes was simply a thickened milk in which one could not recognize separate curds on testing it. In that which was stirred the milk showed a distinct tendency to separation into a paler solution containing small easily visible and tastable, rather firm curds, about the size of a pin-head. In the boiled, fat-free milk beakers there was the same condition, only the curds were tougher, and the milk was decidedly gritty to the taste in the stirred beaker.

Each of the eight beakers of milk treated as an unknown could at once be recognized and especially *could the stirred milk in each case be distinguished from the unstirred milk on account of the greater distinctness, size and firmness of the curd.*

One can only agree with Czerny that the conditions *in vitro* and in the stomach are probably different, but it would be as easy from this experiment to conclude that motion favors hard curdling, as to deduce from his experiments that curdling is inhibited. Fortunately we do not

need laboratory experiments to convince us that milk can curdle in the stomach in large, hard clots. Those of us who have fed raw milk have repeatedly seen infants with disturbed gastric digestion, if I may use the term, vomit firm, leathery curds larger than the end phalanx of a large thumb. Czerny probably has not seen these large stomach curds because he uses boiled milk exclusively.

It seems to me, then, quite plausible that tough curds are formed in the stomach of an infant when fed raw milk; experimentally, in a healthy infant when the casein is excessive and especially when undiluted, and clinically in a dyspeptic infant when its tolerance for raw casein is overstepped, no matter how small an amount is given; and that these hard curds are resistant to digestive liquefaction and pass through the intestinal tract without complete disintegration. This is evidenced by the fact that the curds, when there is considerable diarrhea, are passed through rapidly and are abundant and whiter and softer, and when the baby is constipated they are more yellow and always harder, as if they had had a longer time to express whey content and also a more prolonged exposure to the digestive juice, leading to a reduction in size. These harder curds often look as if they had had holes digested into them while the softer ones are nearly always more rounded and even.

Tobler has stated that "it is highly improbable that such a casein mass should pass through the whole intestinal tract undigested." It is hard to see why such tough curds as we have seen in the test-tube and as we have seen vomited from an infant's stomach, should not pass through as undigested as other pieces of all kinds of solid food, that we are familiar with in infant and adult. It is quite inconceivable, it is true, that any casein curd from boiled milk could pass through undigested.

That such large bodies can easily pass the pylorus is shown in the cases where pennies, safety-pins, marbles and what not are passed.

That the presence of hard curds in the stools is due to the formation of large curds in the stomach seems further highly probable when we know that they will disappear as well when enough sodium citrate is added to the milk as when it is boiled (see case of Baby W.). Milk treated with sodium citrate acts in the test-tube like boiled milk as far as coagulation is concerned, and it is reasonable to assume that it is the lack of firm coagulation in the stomach that causes the curds to disappear in both cases.

German pediatricians use boiled milk in feeding their babies. We, in America, use raw milk almost as much, as a routine, as they do boiled milk. How deeply the hobgoblin of scorbutus has influenced us is shown even in the attitude of the mothers, who immediately wonder if they have called the right physician to see the baby if he asks to have its milk boiled, even if only for a few days. It seems to me then, that, for the above

reasons, we are justified in concluding that these hard curds do not occur in Germany while they are not uncommon with us. If they did occur there they long ago would have been accurately described (and the descriptions of "casein masses" by German clinicians are certainly indefinite now as compared with Talbot's and mine), they would have been analyzed, their origin determined and the present controversy would not have been continued nor so heated. The very impatience with which Meyer and Leopold deny all that Talbot claims, while it seems so plausible to us, can hardly be explained on any other basis than that they do not see these hard curds as we do.

Hard curds, are, furthermore, evidently a digestive disturbing factor, and the arguments of Meyer and Leopold, based on metabolism, to show the harmlessness of casein, are wholly beside the question. It is easy to agree with these observers that boiled casein produces no digestive or metabolic disturbance that is recognizable at present, but raw casein in milk can produce a digestive disturbance, in that hard curds may occur when it is fed.

The question of protein digestion, so recently settled for many of us by Heubner, Czerny and Finkelstein, and their schools, if the above conclusions are warranted by the evidence, must be opened again. As shown above, when hard curds appear in the stools, depending wholly on the baby or on the amount of casein given in raw milk, other evidences of indigestion commonly appear. If the same food is boiled, commonly all of the symptoms of indigestion disappear as well as the curds. Whether the curds are an evidence of a primary protein indigestion, secondarily causing mechanical or other irritation; or whether they are an accompaniment of some other digestive disturbance caused by feeding raw milk, just as mucus, curds, increased peristalsis, etc., accompany, say, a dose of castor oil, remains to be determined. It seems to me that these hard curds must be given the same weight as an evidence of casein indigestion that is given to the small soft curds, as an evidence of fat indigestion, although the two processes are wholly different.

Practically, that is, clinically, one's conclusions concerning protein digestion in feeding cow's-milk are but little influenced by the evidence that I have presented, that under certain limited conditions casein may appear undigested in the infant's stool as hard curds. In the experiments that I have given the hard curds were in reality an artefact. Even in the use of diluted, raw, whole milk mixtures as commonly used, these curds rarely appear unless the baby is given a larger amount of milk than it should have; i. e., when a baby is improperly fed. Indeed, even when hard curds appear, under these conditions, it is probable in many cases that the fat or the carbohydrate has produced an indigestion, and the hard curds are simply a result of an increased peristalsis that has

swept them through before they could be digested completely. The appearance of these hard curds, when proper amounts of raw milk are used, will be limited very largely to those patients who are getting fat-free milk, and to a very small percentage of patients in whom, for some reason, there is a peculiar temporary susceptibility to casein indigestion. There is some evidence in my experience that raw milk will at times produce colic, or discomfort that is relieved by boiling the milk. Even in an adult I have known 24 ounces of raw milk repeatedly to produce colicky pains and even a slight diarrhea, while the same amount of boiled milk under identical conditions never causes discomfort. Even when raw milk is used in therapeutic amounts, we must conclude, in spite of these isolated cases, that the dictum that casein produces neither digestive nor metabolic disturbance is very nearly true. Certainly it would be wholly unjustifiable to speak of it as belonging, as a disturbing factor in infant feeding, even remotely in the same class as the fat or the sugar.

In this paper I am offering no therapeutic suggestion of any kind with reference to whether milk should commonly be boiled or not. I cannot refrain from saying a word, however, concerning certain therapeutic measures. Certain very diverse foods, commonly recognized as easily digested foods, such as buttermilk, condensed milk, dried milks, sodium citrated or otherwise alkalized milks, all have one thing in common—they do not curdle in hard masses as raw milk does.

On the other hand, it is certainly a question whether the use of rennin, as in pegin, or chymogen, has decided, or, indeed, any advantages when the milk is previously boiled, over boiled milk itself; and when not boiled the result is not satisfactory because of the toughness of the small curds that are formed.

Even in the preparation of *Eiweissmilch*, with raw and boiled milk, respectively, there is an appreciable difference in the consistency and amount of the curd and the amount of whey extracted; hence a difference in the ultimate food itself in the very respect that makes it unique and effective as a therapeutic measure. He who uses raw *Eiweissmilch* will get very different results from another who uses boiled milk in its preparation. The fact that Finkelstein, Langstein and Meyer make no reference to whether boiled or raw milk should be used in preparing this food, shows how little German pediatricians appreciate this great difference between raw and boiled milk, or rather how unfamiliar, *practically*, they are with the use of raw milk as an infant food and with the one evident digestive disturbance that it occasionally causes, i. e., the formation of hard curds.

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REFERENCES

Talbot, F. B.: Composition of Large Curds in Infants' Stools, *Boston Med. and Surg. Jour.*, June 11, 1908, p. 905; The Composition of Small Curds of

Infants' Stools, *Boston Med. and Surg. Jour.*, Jan. 7, 1909, p. 13; Casein Curds of Infants' Stools, *Arch. Pediat.*, December, 1910, p. 919; Casein Curds in Infants' Stools, Biologic Proof of their Casein Origin, *Arch. Pediat.*, June, 1910, p. 440.

Meyer, L. F., and Leopold, J. S.: On the So-called Casein Masses in Infants' Stools, *Arch. Pediat.*, October, 1909, p. 773, and February, 1910, p. 126.

Southworth, T. S., and Schloss, O. M.: The Hard Curds of Infants' Stools; their Origin, Nature and Transformation, *Arch. Pediat.*, April, 1909, p. 241.

Czerny, A.: *Des Kindes Ernährung, Ernährungs-Störungen, und Ernährungs-Therapie*, 1909; Franz Denticke, Leipsic and Vienna.

Langstein and Meyer: *Säuglingsernährung und Säuglingsstoffwechsel*, 1910; J. F. Bergman, Wiesbaden.

Finkelstein, H., and Meyer, L. F.: Ueber Eiweissmilch, *Jahrb. f. Kinderh.*, May and June, 1910.

A DUODENAL TUBE FOR INFANTS

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During the past few months two tubes have been devised which may be introduced by mouth and passed into the stomach and thence into the duodenum. The description of these tubes was published almost simultaneously by Gross¹ and by Einhorn.² Both instruments, however, were constructed for use on adults, and both seem to have accomplished their purposes, although they differ somewhat in principle. It seemed to me that it would be well worth while to devise a similar tube for infants, and accordingly I have endeavored to modify and, as I believe I can demonstrate, have succeeded in so modifying the Gross tube that it can readily be adopted for use in the field of pediatrics. I believe that this tube will be of practical use in the treatment of infants, and may serve also to give additional information in those unexplained cases of malnutrition with which we constantly are confronted.

In this paper I do not intend to do more than give a simple description of the tube, to prove that it in reality reaches the duodenum, to describe its method of introduction, and in the briefest way, to indicate its possible uses. In a subsequent article I hope to consider in detail its clinical application, and to report on the duodenal juice in infancy in normal and pathologic conditions, a study that is now under way. The principle of the duodenal tube which I present consists in having a heavy metal ball attached to the end of a very light tube so that it will be quickly carried by the aid of gravity through the stomach and the pylorus.

The tube shown in the accompanying illustration (Fig. 1) is made of very soft, light rubber, 5 mm. in diameter, and has at one end a silver-plated lead ball. The ball is perforated by numerous small openings and one large central one, and is covered over by the end of the tube, which has corresponding perforations. The diameter of the rubber-covered metal ball is 9 mm.

In this connection I would say that I found it most difficult to ascertain the size of the lumen of the pylorus in the various ages of infancy. The figures given in studies on this subject, for example that of Pfaundler, have as a basis measurements made on the cadaver, and have the usual limitations of statistics obtained in this way. By trying balls of different sizes I found that one of 9 mm. gave in general the best results. A ball

1. Gross, M.: Jour. Am. Med. Assn., April 23, 1910.

2. Einhorn, M.: Med. Rec., New York, Jan. 15, 1910.

of 6 mm., for instance, will not be carried so quickly through the pylorus by gravity and takes a longer time to enter the duodenum.* Beside the tube, I used the same glass collecting bulb which is made use of with the tube for adults.

TECHNIC

The preparation of the infant for duodenal aspiration consists merely in enveloping it snugly in a sheet or in a blanket in such a way that the hands cannot be freed to grasp the tube. The time most suited for introducing the tube, if an uncontaminated juice is desired, is two or three hours after the last feeding; that is, when the stomach is empty. If it is not performed, for one reason or another, at this time, and if the infant has just been fed, I have found it of advantage to empty the

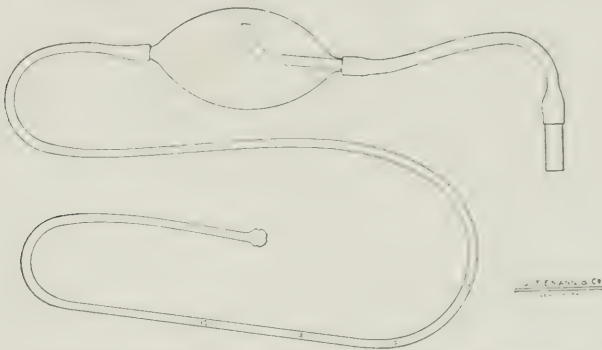


Fig. 1.—Duodenal tube for use in infants, with metal ball and glass bulb, for aspiration and collection of duodenal juice.

stomach with an ordinary stomach-tube as a preliminary step, and in this way avoid all possibility of clogging the small holes in the ball by means of milk coagula. The tube is introduced with the infant held in the sitting position, the method being in no way different from that followed in passing the stomach-tube. The advent of stomach contents, milk or gastric juice will inform us when the ball has reached the stomach; this will be found to be when it is about 18 to 20 cm. distant from the lips. The child is now placed on its right side, and the tube introduced 5 cm. farther, until the 25 cm. mark is at the lips. From this point on, the object is to feed the tube little by little until it reaches and passes the pylorus. If it is fed too fast there is danger of its doubling on itself, with failure as the result. In this regard a little practice is necessary, but after a few attempts a sense of precision is gained. If the tube is pushed farther every few minutes the peristaltic action of the stomach will be felt to aid

*Smaller infants frequently cannot swallow the larger ball, and we have to resort to the 6 mm. ball, which gives the same result, but is more easily clogged by the viscid juice or extraneous particles.

in carrying it along. After fifteen minutes the 30 cm. mark should be at the lips, and about ten minutes later, it should have advanced to between 30 and 35 cm., which means that it is in the duodenum. No rigid schedule can of course be outlined in this connection. I have reached the duodenum within ten minutes and usually am able to enter it within twenty minutes after I have introduced the tube. In one very small, weak infant, I failed to pass the tube.

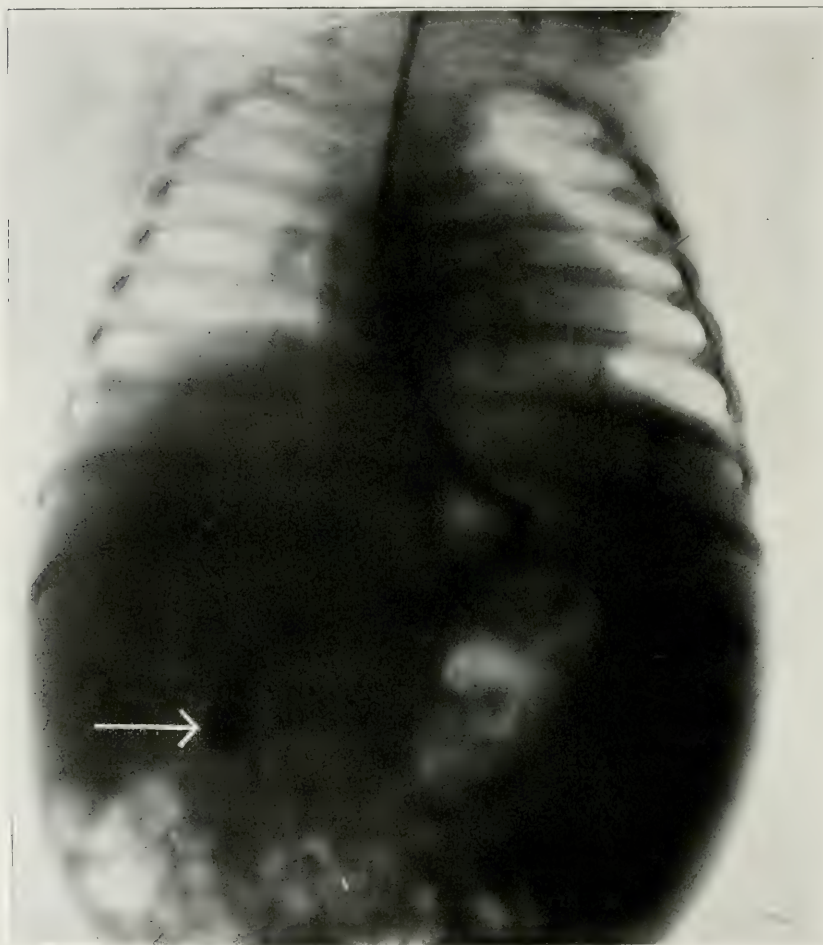


Fig. 2.—Radiograph showing tube and metal ball well within the duodenum as indicated by the arrow.

The first question generally asked is: How do we know that it is in the duodenum? Before answering this I wish to refer to the two plates (Figs. 2 and 3) which are taken from radiographs kindly made for me by Dr. Hirsch, of a 4 year-old infant on the service of Dr. Huber, in Beth

Israel Hospital. The first (Fig. 2) shows the tube and metal ball well in the duodenum, having curved down into the upper intestine after traversing the stomach. For the purpose of obtaining a clear shadow a small rubber tube infiltrated with lead was inserted into the duodenal tube before it was passed on the infant. In order to dispel any doubt as to the whereabouts of the end of the tube, after this radiograph was taken I then poured a suspension of bismuth in milk along the tube into the stomach. Figure 3 shows the stomach partly filled with this bismuth, which has within a few minutes passed also into the duodenum, and portrays the ball of the tube in the duodenum as in the previous radiograph. These pictures are conclusive; they prove that a tube can be passed through the mouth into the intestine of an infant. However, the character of the juice which is aspirated will also generally give the signal that the duodenum has been reached. At first, when the tube is in the stomach, the aspirated fluid is markedly acid to litmus, and contains flocculi of milk. It may become still more acid if the secretion of gastric juice is stimulated. When the ball reaches the duodenum, the juice becomes less acid, the acidity gradually diminishing until it becomes neutral or slightly alkaline. Generally it has a characteristic viscid consistency and a yellowish or greenish tinge, which is rather difficult to perceive by artificial light. This color is due to a mixture of bile, and varies from a golden yellow to a tinge of yellow or green; or the fluid may be colorless although the tube has passed through the pylorus, and its end lies beyond the papilla of the bile duct. The fluid is generally not absolutely clear, but contains small flocculi which tend to fall to the bottom of the glass as sediment. The characteristic fluid, the only fluid which we can use as a criterion that we are in the duodenum, is one that is neutral or alkaline, and shows a definite yellow or green color.

In the accompanying illustration (Fig. 1) it will be noted that a glass bulb is attached to the outer end of the tube, and that this again has a small piece of tubing attached to it. This bulb is to serve as a container for the juice that is collected, and the tube at its end is for the purpose of aspiration.

The aspiration may be made by the mouth, the method that I have followed, or by means of a syringe. Aspiration is generally necessary, as the juice does not at all times flow freely, and the tube may be choked by particles of milk. This procedure should be carried out gently and not too often, as it has a tendency to cause retching and gagging. As can be imagined, there are many minor details of technic which might be mentioned, but the mode of introduction is simple, so that these finer points may be left to suggest themselves to those who make use of the tube.

A word as to the discomfort which the passage of the tube entails. I need not mention that it can cause no injury, for we all acknowledge that the stomach tube is used with perfect safety and the soft duodenal tube, in this respect, can be, and is in no way different. I have passed the tube in infants varying in age from 2 months to 14 months (the smallest infant weighed 7 pounds) and found that it did not cause much discom-

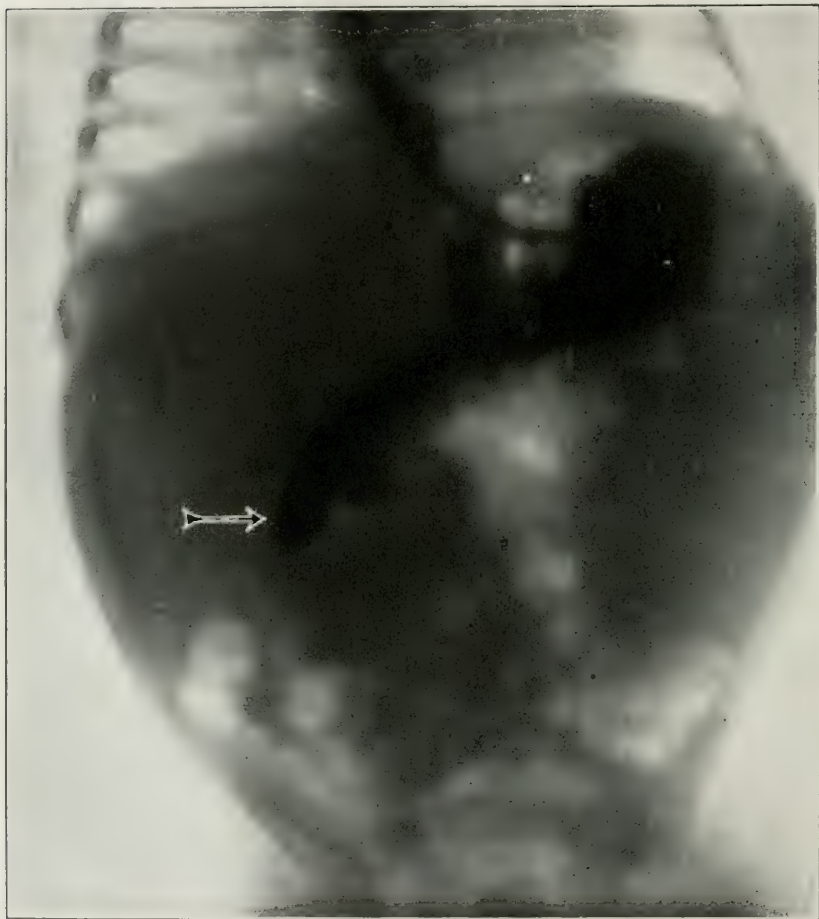


Fig. 3.—Radiograph showing stomach filled above with air and below with bismuth mixture, which has also entered the duodenum. The arrow indicates the position of the ball at the end of tube within the duodenum.

fort. Some of the older infants were constantly annoyed by it, but far more often the babies did not seem to be aware of its presence, and frequently sucked it as they do a pacifier, dozing all the while. The child, of whom I show the radiographs, fell fast asleep about ten minutes after the tube was inserted.

PURPOSES FOR WHICH THE TUBE MAY BE USED

I have remarked that the first question generally asked has been as to how we are to know that the tube is in the duodenum; the second has been as to the application of the tube. It is very difficult to state the scope of any new instrument or method. It is doubtful whether the stomach-tube seemed to be of great value when it was first suggested. I candidly admit that I cannot fully answer this question, and clearly define the value of the duodenal tube for infants. It seems to me, however, that it may well be of value in studying the physiologic or pathologic processes of digestion. Intestinal fistulas have always been prized as rare opportunities, especially in early childhood, for such investigations, and here we have a method of stimulating, to a certain extent, such a fistula. It would seem worth while, to mention merely one subject, to ascertain whether the duodenal juice containing, as it does, the various ferments of the pancreas and of the upper intestine, is the same in normal infants and in cases of marked malnutrition. This is a phase which I hope later to report on. There are many other pathologic problems which its use may help to solve; for example, the secretion of bile in icterus of the newborn; pharmaceutic problems, as for example, the excretion of drugs through the bile; or the effect of drugs on the glandular secretions; dietetic studies; for example, the influence of certain food stuffs on the quantity or quality of the ferments. These and many other investigations may be undertaken by this method.

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SPASM OF THE PYLORUS IN INFANCY

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CHRONIC GASTRIC INDIGESTION

Everyone who sees many sick infants is familiar with the symptomatology of chronic gastric indigestion at this age. It seldom occurs in the breast-fed, but develops, as a rule, after a longer or shorter period of bad artificial feeding. Vomiting is the most prominent symptom, occurs without any definite relation to the time of taking food and is never explosive. The amount of the vomitus rarely exceeds that of the food taken at the last feeding and the vomitus usually shows evidences of disturbance of the gastric digestion. The stools often present the evidences of an associated intestinal indigestion, but constipation, as the result of the reduction in the amount of food retained, is not uncommon. The stools are, however, never of the starvation type, but show by their characteristics that food is passing from the stomach into the bowel. There is never any visible peristalsis and, of course, no tumor to be felt at the pylorus.

HABITUAL VOMITING

Another not very uncommon condition is that in which a baby, without any other symptoms of indigestion, vomits habitually and yet gains steadily and appears normal in every other way. This is often, especially in the breast-fed, due simply to an excessive amount of food. In both the breast-fed and the bottle-fed, however, it is probably more often due to the imperfect closure or lack of tone of the cardiac orifice. This is shown by the facts that vomiting rarely takes place when they are quiet and that it varies with the amount of exertion and the position of the baby. The vomiting is never explosive and the vomitus shows no evidences of indigestion. There is, of course, no visible peristalsis or palpable tumor. The following case is a good example of this condition:

Anne A. was born at full term June 11, and weighed 7 pounds. She was nursed for a few weeks. She vomited a good deal but had normal movements. The milk then gave out and the child was put on a home modification of cows' milk. She continued to vomit, although various modifications, including whey mixtures, were tried. The percentages of fat had never been excessive but had never been low. None of the mixtures had been very highly alkaline. Variations in the length of the intervals and in the amount of food had made no difference in the vomiting. The vomiting occurred at any and all times, sometimes even just before a feeding. She never vomited during the night. The vomitus never contained bile. The bowels moved regularly, the stools being of good size and well digested. She was happy, active, and seemed well. She had gained regu-

larly but slowly in weight, weighing when she was seen, September 29, 10 pounds and 8 ounces. The physical examination showed nothing abnormal in any way. Variations in the composition of the food, including low percentages of fat and high alkalinity, made no difference in the vomiting, which, however, gradually diminished and finally ceased when she was a year old. At the age of nearly 3 years she was perfectly well.

SPASM OF THE PYLORUS

The symptomatology of spasm of the pylorus is materially different from that of the two conditions just mentioned, so different that the diagnosis from these conditions ought always to be possible. In the majority of instances the babies are of the excitable, irritable and neurotic type. It occurs in both the bottle-fed and the breast-fed, but more often in the former than in the latter. The symptoms seldom appear immediately after birth, but usually develop in the first few weeks, although they may not manifest themselves until the baby is some months old. The symptomatology of this condition varies considerably according to the amount of spasm present in the individual instance.

In the milder cases there is frequent vomiting, which is at times explosive and at others not. It is often preceded and accompanied by evidences of gastric pain and distress. The amount of material vomited does not ordinarily exceed that taken at the last meal. The vomitus shows, as a rule, little or no signs of disturbance of digestion. There is a tendency to constipation, but the stools show plainly that a considerable proportion of the food ingested passes through the pylorus into the intestine. The disturbance of nutrition is not extreme. The following case is a good example of this type:

Catherine D. was born February 17. She was started at once on eleven feedings of 2 ounces of a mixture of one part of whole milk and two parts of barley water. She continued to take this until March 19, when she was given ten feedings of 2½ ounces of a mixture containing 2 per cent. of fat, 5 per cent. of milk sugar, 0.75 per cent. of whey proteids and 0.25 per cent. of casein, with lime water equal to 10 per cent. of the total quantity. The child was seen March 27. She was said to have vomited after every feeding since birth. She had vomited large amounts, so that very little was retained. The vomiting had been explosive. Water was vomited the same as milk. The bowels had always been constipated.

The child was small but fairly nourished and of good color. The skin was in good condition. The anterior fontanelle was level. The posterior fontanelle and the sutures were still open. The heart and lungs were normal. The level of the abdomen was a little above that of the thorax. There was no bulging of the epigastrium. There was no visible peristalsis, even on flicking the abdomen, and no tumor was felt. The examination showed nothing else abnormal. She weighed 2,580 grams.

The stomach was washed out and found to contain considerable curdled milk and mucus. There was no visible peristalsis and no tumor was made out, even when the stomach was full of water.

She was given twelve feedings of 45 c.c. each of whey. She vomited after about half of her feedings, but the vomiting was never explosive. The amount of the vomitus varied considerably. The stools were small and green, and were composed mostly of mucus although they contained a few fine curds.

The stomach was washed out again on March 30, half an hour after a feeding. The stomach was empty, although she had not vomited more than a teaspoonful after the feeding. There was no visible peristalsis, even when cold was applied to the abdomen. No tumor was felt either when the stomach was full or when it was empty, although the abdominal walls were lax. The amount of whey was increased to 60 c.c. at each feeding.

April 2 the child was given ten feedings of 60 c.c. each of a mixture containing 1.50 per cent. of fat, 7 per cent. of milk sugar, 0.75 per cent. of whey proteids and 0.25 per cent. of casein, with lime water equal to 25 per cent. of the cream. The vomiting then increased in both frequency and amount, but the stools began to show a little fecal matter.

The amount of food was increased to 75 c.c. April 4. The application of flaxseed poultices to the epigastrium for twenty minutes before and after each feeding was begun at this time and four days later the administration of 1/80 of a minim of the tincture of opium twenty minutes before each feeding was started.

The strength of the food was gradually increased, so that on May 16, when the child was last seen, she was taking ten feedings of 90 c.c. each of a mixture containing 3 per cent. of fat, 7 per cent. of milk sugar, 0.75 per cent. of whey proteids and 0.50 per cent. of casein, with lime water equal to 25 per cent. of the milk and cream. She was vomiting a little after about half of the feedings and the vomiting was at times explosive. She was, however, having three or four stools daily, which were of fair size, greenish-yellow in color, and contained some small curds. At no time was there any visible peristalsis or tumor. She had increased in weight up to 3,040 grams.

The child was alive and well when 3½ years old.

In the more severe cases there is visible peristalsis in addition to the symptoms already mentioned as characteristic of the milder type. These symptoms are more marked than in the mild cases, the stools show less fecal residue and the disturbance of nutrition is much greater. There are numerous instances of this type on record, among which may be mentioned those of Koplik,¹ Case 2; Griffith²; Ibrahim,³ Cases 4, 5 and 7; Pease⁴; Rosenstern,⁵ Case 2; and Engel,⁶ Cases 1 and 2. It is probable that many of the cases of Heubner,⁷ Finkelstein,⁸ Hutchison⁹ and others, which have been reported as cases of congenital hypertrophic stenosis of the pylorus with recovery under medical treatment, belong in this class. Many of these cases show signs of motor insufficiency for a long time. The following cases are good examples of this type:

Winthrop B.¹⁰ was born May 21, and weighed 10 pounds. His mother tried to nurse him but had practically no milk, so that at the end of two weeks he

1. Koplik: *Am. Jour. Med. Sc.*, 1908, cxxxvi, 1.

2. Griffith: *Arch. Pediat.*, 1905, xxii, 721.

3. Ibrahim: *Die angeborene Pylorusstenose im Säuglingsalter*. S. Karger, 1905; *Therap. Monatsh.*, 1908, xxii, 560.

4. Pease: *Lancet*, London, 1909, ii, 1280.

5. Rosenstern: *Deutsch. med. Wchnschr.*, 1910, xxxvi, 31.

6. Engel: *Deutsch. med. Wchnschr.*, 1909, xxxv, 1271.

7. Heubner: *Die Therapie der Gegenwart*, 1906, viii, 433.

8. Finkelstein: *Jahrb. f. Kinderh.*, 1896, xliii, 105.

9. Hutchison: *Clin. Jour.*, 1908, xxxii, 343; *Brit. Med. Jour.*, 1910, ii, 1021.

10. Morse: *Boston Med. and Surg. Jour.*, 1906, clv, 343.

weighed but 9 pounds. He was then given various modifications of milk but did badly, having much colic and many bad movements, but no vomiting. He lost weight rapidly and got into such a serious condition that a wet-nurse was procured August 1, when he was 2½ months old. Her milk was, however, insufficient, so that he continued to lose weight, although his digestion was good. A variety of foods were then tried, on none of which did he do very well. Vomiting appeared first August 25. He continued to vomit and did not gain, although his stools were normal. Another wet-nurse was procured September 27. The vomiting gradually increased, nevertheless, although he continued to have good-sized, well digested stools. There was no nausea, the milk coming up in gulps without effort. The vomiting was never explosive. It usually occurred soon after nursing, but he often spit up considerable amounts just before the time for the next feeding. He was seen October 15.

The child was small and thin but his color was fair, his skin supple and his muscles strong. The level of the abdomen was the same as that of the thorax. The stomach was not enlarged to percussion. Occasional waves of contraction could be seen running over the stomach from left to right. No tumor could be made out in the region of the pylorus. The rest of the physical examination showed nothing abnormal. He weighed 11 pounds.

The breast-milk was continued, the baby being fed at three hour intervals and being given three or four teaspoonfuls of lime water at each nursing. The vomiting continued, however. It usually occurred about three, ten and twenty minutes after each nursing, but often recurred just before the next nursing. The bowels moved but once in thirty-six or forty-eight hours, but the stools were of good size and well digested. There was no visible peristalsis after November 1, and no tumor was ever found.

The vomiting gradually diminished and by the time he was a year old had entirely ceased. He gained slowly during November but after that put on weight rapidly. Breast feeding was continued until he was 14 months old, when he weighed 28 pounds and was perfectly well in every way.

He swallowed a cent when 2½ years old. It went through him in twenty-four hours. At the age of 6 years he was perfectly well.

Edwina W. was born July 8 and weighed 13 pounds. She was not nursed but was given various proprietary foods and milk modifications, none of which agreed. She began to vomit when she was only a few hours old. She did not vomit every day but would vomit frequently for several days, would then go two or three days without vomiting, and so on. She seemed perfectly normal between the attacks, took her food eagerly and retained it apparently without discomfort. She sometimes vomited what was apparently two or three times the amount of food taken at the last feeding. The vomitus was sour and contained curdled milk but no mucus. There was no relation between the time of the vomiting and that of the feeding. She vomited with some difficulty, often straining a good deal. She had frequent attacks of colic, which were not associated with vomiting, and belched much gas. She had from three to five stools a day, normal in color, amount and consistency. She had gradually lost weight; when seen, August 19, she weighed only 3,360 grams.

The child was fairly developed and nourished. The stomach reached 2 cm. below the navel. Slow peristalsis from left to right was distinctly visible. No tumor was felt. She was discharged from the hospital September 22. At that time she was vomiting but once or twice a day and sometimes went several days without vomiting. The vomiting was at times explosive, but was more often regurgitation. She at first had from three to seven small, brownish-green stools, composed largely of mucus, daily. The stools began to be yellow and to contain a few curds August 26. Early in September the stools became yellow, sufficient in amount and well digested, both macroscopically and microscopically. Peris-

talsis was at times visible up to the time she was last seen. No tumor was felt at any time. Her weight, September 22, was 3,580 grams.

The food given in this infant's case was as follows:

August 19.—Whey, twelve feedings, 2 ounces each.

August 22.—Fat, 0. per cent.; milk sugar, 7 per cent.; whey proteids, 0.90 per cent.; casein, 0.25 per cent.; lime-water equal to 20 per cent. of the milk; eight feedings, 3 ounces each.

August 25.—Fat, 0.75 per cent.; milk sugar, 7 per cent.; whey proteids, 0.90 per cent.; casein, 0.50 per cent.; lime water, 20 per cent. of the milk and cream; eight feedings, 3 ounces each.

August 27.—Fat, 1.25 per cent.; milk sugar, 7 per cent.; whey proteids, 0.90 per cent.; casein, 0.25 per cent.; lime water, 20 per cent. of the milk and cream; eight feedings, 3 ounces each.

August 30.—Fat, 1.75 per cent.; milk sugar, 7 per cent.; whey proteids, 0.90 per cent.; casein, 0.50 per cent.; lime water, 20 per cent. of the milk and cream; eight feedings, 3 ounces each.

September 14.—Fat, 2.25 per cent.; milk sugar, 7 per cent.; whey proteids, 0.90 per cent.; casein, 0.50 per cent.; lime water, 20 per cent. of the milk and cream; eight feedings, 3 ounces each.

The patient was seen again when 6½ months old. She was then perfectly well, did not vomit, and had normal movements. Her mother said that she had not seen any peristalsis for a long time. She was in very good general condition. The abdominal examination showed nothing abnormal.

Some of these infants die and no thickening of the pylorus or narrowing of its lumen is found on post-mortem examination (Cautley,¹¹ Carpenter¹²), thus proving beyond a doubt the existence of this condition. The majority recover under breast or careful artificial feeding and medicinal treatment. The visible peristalsis may persist for weeks or months after the cessation of the vomiting. It was noted in one of Ibrahim's patients (Case 6) for four months.

In the most severe cases there is also a palpable tumor at the pylorus (Rob¹³; Clowes¹⁴; Hutchison; Carpenter; Rosenstern, Cases 1, 3 and 4). This tumor is usually small in comparison with that felt in congenital hypertrophic stenosis of the pylorus. It is variously described by different authors. Koplik describes it in one of his patients (Case 3) as a "thin, cord-like structure" and later as "large as a bean," and in another (Case 1) as "soft and cord-like," while Clowes describes it as "the size of the end of the thumb." Ibrahim states that in one of his patients (Case 6) it was 3 cm. long and that it could be felt to contract and relax. In one of my patients, who is still under observation, it seems about 2 cm. long and 1 cm. thick and can be felt to contract and relax. The authors unfortunately give practically no data as to how long the tumor was palpable in these cases, merely stating that the patients recovered, leaving it to be assumed that the tumors disappeared. There are no records, as far as I am aware, of autopsies on infants in whom a tumor

11. Cautley: *Brit. Jour. Child. Dis.*, 1908, v, 179.

12. Carpenter: *Lancet*, London, 1908, i, 779.

13. Rob: *Lancet*, London, 1906, i, 1751.

14. Clowes: *Lancet*, London, 1908, ii, 534.

was palpable, to show that the tumor really disappeared. Autopsies in several of the cases which have been reported as instances of this condition have, however, shown definite thickening of the pylorus (Bloch¹⁵; Ibrahim, Case 3; Batten¹⁶). This fact, of course, makes the accuracy of the diagnosis in these cases somewhat doubtful.

THE RELATION BETWEEN SPASM OF THE PYLORUS AND CONGENITAL
HYPERTROPHIC STENOSIS OF THE PYLORUS

The questions immediately arise as to the relation between these cases of pyloric spasm with palpable tumor and mild cases of congenital hypertrophic stenosis of the pylorus, and the part which spasm plays in the etiology and symptomatology of congenital hypertrophic stenosis of the pylorus. It will be better, perhaps, to consider the latter questions first. There has been, and still is, much difference of opinion as to the part which spasm plays in the etiology of congenital stenosis of the pylorus, some claiming that it is the direct and sole cause of this disease; others that it has no part in its development. The weight of the evidence seems to prove, however, that stenosis of the pylorus in infancy is a congenital condition and that spasm plays no part in its causation, either before or after birth. The strongest points in favor of the congenital origin of the stenosis are the facts that the condition has been found in the fetus, that the symptoms not infrequently appear immediately after birth and that the hypertrophy is largely local.

Cautley's arguments seem to show conclusively, moreover, that spasm cannot be the cause of hypertrophy. They are in brief as follows: Spasm of the pylorus may occur at any age. It is not an affection peculiar to the first months of life. There is no proof of the development of hypertrophy of the pylorus at other ages as the result of spasm. There is no evident reason why spasm of the pylorus should cause hypertrophy in infancy when it does not at other ages. Pyloric spasm may prove fatal in infancy without causing hypertrophy. There is no analogous hypertrophy in other parts of the alimentary canal as the result of spasm. Prolonged anal spasm does not cause it. The pylorus is normally in a state of contraction. It dilates to allow the passage of the gastric contents in response to stimuli from the duodenum. It does not seem reasonable that the amount of spasm sufficient to oppose the stimulus to dilatation can be great enough to produce the excessive hypertrophy of the circular muscular fibers so constantly present. If the hypertrophy is due to spasm the longitudinal fibers should be as much hypertrophied as the circular, but they are not. Further evidence that the hypertrophy is not due to spasm is that the hypertrophy does not disappear after gastro-enterostomy

15. Bloch: *Jahrb. f. Kinderh.*, 1907, lxx, 337.

16. Batten: *Lancet*, London, 1899, ii, 1511.

(Morse, Murphy and Wolbach¹⁷). It is evident, therefore, that primary pyloric spasm and congenital stenosis of the pylorus are two independent conditions.

Although pyloric spasm and congenital hypertrophic stenosis of the pylorus are unquestionably distinct entities, there is no doubt that spasm plays an important part in the production of the symptoms in many cases of pyloric hypertrophy. In this way only can the sudden onset of the symptoms be explained in many instances in which marked hypertrophy is found at operation. The following case is an example of this type:

Arthur H. was seen when five weeks old. He was born two weeks before he was expected and weighed 4 pounds and 14 ounces. He was breast-fed from the start and had been perfectly well except for a considerable amount of colic. He had not vomited and the stools had been normal until September 7, four days before he was seen. He had gained $1\frac{1}{2}$ pounds.

The mother began to menstruate September 7. The baby vomited at once. The first vomitus contained a little bile. His stool that morning was of good size and well digested. The nursing was stopped and he was given water only. He was also given some castor oil. He retained the castor oil but vomited the water.

He was given nothing except a little brandy and water on the eighth and did not vomit. The nursing was begun again on the ninth. He was given a little water before the nursing and the duration of the nursing was limited to $2\frac{1}{2}$ minutes. He began to vomit again after seven or eight hours.

September 10 he was given one ounce every $1\frac{1}{2}$ hours of a mixture of 1 ounce of skimmed milk, $1\frac{1}{2}$ ounces of lime water and 8 ounces of water. The vomiting persisted and the amount was reduced to half an ounce at a feeding. This was also vomited, so that for the twenty-four hours before he was seen, September 11, nothing at all had been retained. The bowels had been moved by enemata. The stools had consisted of green mucus. The vomiting had been projectile.

The child was small and thin but in fair condition. His color was good. The examination showed nothing abnormal except in the abdomen. The ingestion of half an ounce of water was followed by marked visible gastric peristalsis, running from left to right. A tumor, the size of a small marble and moderately movable, was felt in the region of the pylorus. A stool, which was seen, was small, loose, greenish-brown in color and composed almost entirely of mucus.

Gastro-enterostomy was done the same day by Dr. C. L. Scudder, who found a tumor at the pylorus the size of the last phalanx of the thumb. He has done uninterruptedly well since the operation, five months ago.

In many cases of slight or partial stenosis of the pylorus, the symptoms in considerable part are undoubtedly due to the spasm. When the spasm is relieved by appropriate treatment the symptoms diminish and in mild cases disappear. A large proportion of the reported cures by medical treatment of cases of pyloric stenosis in which distinct tumors have been felt are undoubtedly to be explained in this way (Batten; Bloch; Ibrahim, Case 3; Rosenstern, Cases 1, 2 and 3; Finkelstein; Heubner, et al.). In fact, no other explanation seems possible, because the evidence at autopsy in "recovered" cases (Ibrahim, Case 3; Batten; Bloch) shows that the hypertrophy remains many months, at least, after

17. Morse, Murphy and Wolbach: Boston Med. and Surg. Jour., 1908, clviii, 480.

the cessation of symptoms. There is, as far as I am aware, no data based on operative or post-mortem findings, as to the anatomic conditions in these cases years after the relief of symptoms. It is probable, however, that a certain number of the cases of benign pyloric obstruction which develop in the third and fourth decades are the final results of mild cases of congenital pyloric stenosis. Many of these patients also show evidences of motor insufficiency years after the cessation of symptoms (Bernheim-Karrer¹⁸).

DIAGNOSIS BETWEEN SPASM OF THE PYLORUS AND CONGENITAL HYPERTROPHIC STENOSIS

While there is no question that spasm of the pylorus and congenital hypertrophic stenosis of the pylorus are two distinct conditions, the diagnosis between them is at times an extremely difficult one. The onset of the symptoms is the same in both, the vomiting is explosive in both and there is visible peristalsis in both. Constipation and loss of weight are common to both. There is sometimes a palpable tumor in spasm; the tumor is sometimes not palpable in hypertrophic stenosis. In spite of the similarity of the symptoms of the two diseases there should be little difficulty in distinguishing the marked cases of hypertrophic stenosis from those of spasm, because the constipation is never so marked or persistent in spasm as in stenosis and because the tumor in spasm is small and cord-like, not large and hard as in hypertrophic stenosis. Variation in the size of the tumor during examination is practically positive proof that the condition is one of spasm, not of hypertrophy. The difficulty in diagnosis comes between the severe cases of spasm and the mild cases of hypertrophic stenosis, because the difference in the symptomatology of the two diseases is entirely in the degree, not in the kind, of symptoms.

In many instances it is impossible at first to make a positive diagnosis between these two conditions. If the baby is breast-fed the chances are much in favor of hypertrophic stenosis, because spasm is very unusual in the breast-fed while hypertrophic stenosis is equally common in the breast-fed and in the artificially fed. If the baby is artificially fed the chances are even, although if the feeding has been very irrational, spasm is a little the more probable. The absence of a palpable tumor is strong evidence against hypertrophic stenosis but does not positively exclude it, because a good sized tumor has sometimes been found at operation when none was felt before it. It is never safe to conclude that there is no tumor, however, unless the abdomen has been examined with the stomach both full and empty and with the abdominal walls relaxed, if necessary under an anesthetic. If no tumor is felt under these conditions an almost posi-

18. Bernheim-Karrer: *Jahrb. f. Kinderh.*, 1909, lxi, 551.

tive diagnosis of spasm is justified. Examination of the gastric contents is of little or no assistance, because there are very few reliable data as to the chemistry of the gastric contents in these conditions and what few data there are are contradictory. An excessive hyperacidity perhaps counts a little, however, in favor of spasm. Dilatation of the stomach seldom develops in simple spasm of the pylorus and, if it does, is always slight. It develops in a certain proportion of the cases of hypertrophic stenosis but is seldom extreme. The presence of dilatation is, therefore, in favor of hypertrophic stenosis and against spasm. Its absence does not, however, count at all in favor of spasm. Dilatation of the stomach, unless extreme, is very difficult of demonstration in infancy. Too much importance must not be attached, therefore, to what are apparently slight degrees of dilatation. Rapid improvement under medical treatment and regulation of the diet is strong evidence in favor of spasm, but does not positively exclude a mild degree of hypertrophic stenosis complicated by spasm. The most important points in favor of spasm in doubtful cases are, therefore, the absence of a palpable tumor, or, if a tumor is present, its cord-like feel, the presence of intermittent contraction and relaxation of the tumor, and rapid improvement under medical treatment and regulation of the diet.

ETIOLOGY

The etiology of spasm of the pylorus in infancy is very obscure. It is apparently most common in excitable and irritable infants, the offspring of neurotic parents. Some writers believe that the normal muscular hyperirritability at this age predisposes the pylorus to spasm. The mechanical irritation of the food or the chemical products of digestion thus directly or reflexly cause spasm when they would not in later life. Others believe that disturbance of the gastric digestion always precedes and causes the spasm. Some observers have found a hyperacidity of the gastric contents, others have not. Engel believes that a gastrosuccorhea is at the bottom of the trouble. It is safe to conclude, at any rate, in view of the conflicting opinions and the insufficiency of the data, that nothing is known as to the etiology which is sufficiently reliable to serve as a basis for treatment.

TREATMENT

The most important part of the treatment of pyloric spasm is regulation of the diet. The best food is good breast-milk. If this is vomited, it is well to remove a part of the cream and add lime water. The next best food is some modification of cow's milk. It is advisable to keep the percentage of fat low, because fat tends to delay the emptying of the stomach. It is also advisable to give as large a proportion as possible of the proteids in the form of whey proteids, because they are not coagu-

lated by rennin and easily pass the pylorus. An alkali should be added to the milk to neutralize any possible hyperacidity and to delay the coagulation of the casein by rennin and thus favor the passage of the liquid milk through the pylorus. These general principles serve, of course, only as a basis for the preparation of the food, which must be varied to suit the individual baby. Plain whey is very useful in some instances; so also is pancreatization in others.

There is much difference of opinion as to whether the food should be given at short or long intervals and as to the quantity which should be given at a feeding. The most rational way of regulating the interval between feedings is to determine how long it takes the stomach to empty itself in the individual case and to make the interval somewhat longer than this. In general, it is probably better to give small amounts at a feeding, although there are many exceptions to this rule.

Daily lavage with plain water or a weak solution of bicarbonate of soda is of assistance in most cases, although some authors think that it tends to keep up the spasm. Warm applications to the epigastrium are sometimes of assistance. Minute doses of some preparation of opium—for example, 1/40 of a minim of the tincture—given a short time before feeding, sometimes seem to diminish the spasm. Atropin and cocain have also been used for the same purpose. It is also important to keep these babies very quiet, especially immediately after feeding.

Rosenhaupt¹⁹ claims good results in this condition from rectal irrigations of salt solution, basing his treatment on Engel's statement that the cause of the trouble is gastrosuccorhea, and on Benczur's experiments which show that in animals rectal injections of salt solution diminish the secretion of gastric juice. He obtained favorable results in all but one case, but does not state how many patients he treated. Rosenstern claims good results in four cases from the rectal instillation of from 250 c.c. to 400 c.c. of Ringer's solution daily. This method of treatment is, however, so new that it must be regarded as still *sub judice*.

Surgical intervention for the relief of pyloric spasm is seldom either necessary or advisable. Carpenter compares it to tracheotomy for laryngismus stridulus. This comparison is, however, perhaps a little too strong, because experience has shown that babies sometimes die of this condition under medical treatment. Surgical intervention is, therefore, justified in certain extreme cases. An exploratory laparotomy certainly ought to be done in all cases in which there is a reasonable doubt as to whether the condition really is one of spasm and not of hypertrophic stenosis and in which the patients are doing badly under medical treatment.

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19. Rosenhaupt: Deutsch. med. Wehnschr., 1909, xxxv, 1789.

BLOOD TRANSFUSION IN INFANTS BY MEANS OF GLASS TUBES *

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The value of transfusion in infants has been demonstrated in the treatment of hemorrhagic disease of the new-born and in cases of hemorrhage after injuries or operations. That this procedure has not been more frequently and successfully tried in these conditions is probably due to the technical difficulties of the operation in infants, and especially in the new-born infant. The chief difficulty is found in uniting the artery of the donor to the small and inaccessible vein of the infant. The largest superficial veins of a baby's arm are so small that one must resort to the less accessible veins of the thigh which, at the best, are scarcely large enough. However, when once a satisfactory connection is made between artery and vein, a flow of comparatively short duration is sufficient to transfer enough blood for an infant. In a baby weighing 8 pounds, a flow of five minutes corresponds to thirty or forty minutes in an adult.

The ordinary methods of transfusion are adapted to the requirements of adults and cannot be so successfully applied to infants. Babies have been transfused by the method of direct suture and with the Crile and Elsberg cannula, by men experienced in this kind of work. Less skilful operators using these methods sometimes find it impossible to transfuse a small infant. The unsuccessful attempts result from a failure to start the flow of blood rather than an inability to maintain it for a sufficient length of time.

Under these circumstances it seems more practical to use a method on infants which will lessen the mechanical difficulties of connecting the vessels, even if, in a technical sense, it is not so perfect as the ordinary methods in present use.

It occurred to me that the use of coated glass tubes, as suggested by Brewer in 1909, might simplify this problem. With this end in view, I conducted a series of laboratory experiments to determine how this method might be modified to suit the needs of infants.

The results, and not the details, of these experiments will be given in this paper. I wish more particularly to describe in detail the prep-

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aration and use of these tubes in transfusing infants, and to report three cases which will illustrate their practical application.

Some of the experiments were made on dogs, but most of the work was done with cats, because their small and delicate vessels more nearly resemble those of the infant.

EXPERIMENTAL WORK

The usual experiment consisted in first bleeding an animal and then reviving it by transfusion, using glass tubes in various lengths and sizes. The common carotid artery of the donor was joined to the recipient's external jugular vein, or one of its smaller branches. In some cases the femoral vessels were used.

The tubes were made from glass tubing of the smallest sizes, cut into lengths varying from 3 to 8 cm. The ends of these tubes were pointed, and all sharp edges smoothed away in the flame. About 3 mm. from either end the tubes were encircled by a shallow groove. This carried the ligature, with which the vessel was tied over the end of the tube.

Straight tubes proved to be better than curved tubes. They are easier to handle and the blood does not clot so quickly in them. The tendency of the blood to clot was found to increase as the tubes were lengthened and their diameters diminished, but a flow of at least ten minutes could always be obtained with tubes 8 cm. in length and 3 mm. in diameter.

Various materials for lubricating or coating the tubes were tried, such as liquid petrolatum, vaselin, stearin, and paraffin, as suggested by Brewer. Vaseline gives too soft a covering and stearin alone is too hard and rough. Paraffin, 54°, is easy to handle and gives a fairly firm, although rather uneven coating. A mixture of vaselin, paraffin and stearin in 2-2-1 proportions gave the smoothest, hardest covering. Blood ran longer without clotting in tubes coated with this mixture than in those coated with paraffin alone. Of any one material, paraffin was by far the most satisfactory. In the course of the experiments, it was found that blood ran surprisingly well in plain glass tubes, and I am sure that they could be used with a fair chance of success if the coated tubes were not available.

The practice gained in working out the technical details in the laboratory was of great value in performing the actual operation on infants.

TECHNIC

The instruments required in the operation are those of an ordinary dissecting layout, to which are added fine scissors, two pairs of small forceps, at least three mosquito hemostats, and the three small tenacula which come with the Elsberg transfusion cannula.

These fine hooks are indispensable in exposing the lumen of the vein until it has been dilated and the tube inserted. Crile clamps can be used to control temporarily the donor's artery, but a small, light artery clip is needed for the infant's vein.

The tubes can be freshly prepared in a few minutes before each operation. The mixture of vaselin, paraffin and stearin, which looks like wax and might be conveniently so designated, is kept in a glass dish, or better a metal box. I use a shallow box 5 inches long and 2 inches wide. Its cover, when turned up, serves as a handle.

It is well to prepare one or two extra tubes for each transfusion. The dry tubes are placed in the box with the mixture, and sterilized by heating over any convenient flame. The tubes fill by capillary attraction as they sink into the melted wax. One is then taken from the box with a sterile hemostat which grasps it near the middle. By slowly tipping the tube the wax is made to run from end to end until it covers every surface. The excess is then drawn off by touching the end of the tube with sterile cotton or gauze, which quickly absorbs the melted wax. I have found this easier and more certain than the method of shaking the wax out of the tube. The wax adhering to the tube hardens in a few seconds into a smooth, firm coating which is not damaged by careful handling during the operation. Tubes not perfectly coated are dropped back into the box, reheated and treated as before.

In many of the laboratory experiments, the small amount of air which a tube contains was forced into the recipient's circulation ahead of the donor's blood. Although no evil effects were noted, it is safer to eliminate all danger of air embolism by filling the tubes with salt solution. This can be done with a small glass or soft rubber syringe. A convenient substitute for the syringe is a piece of cotton or gauze saturated with salt solution. The salt solution can be squeezed from this into the tube and held there by placing in one end a plug of sterile cotton covered with vaselin. This plug is removed after the tube has been tied into the infant's vein and just before it is connected with the donor's artery.

About 2 inches of the donor's radial artery is isolated in the usual manner under cocain. The infant is lightly anesthetized and the femoral, the popliteal, or the long saphenous vein is exposed in the thigh. In the cases here reported, the saphenous vein was not readily found, and the dissection was at once carried down to the femoral vein. This vein is of fair size but rather awkwardly placed on account of its depth. If possible, at least an inch of the vein should be freed. It is then clamped above and tied below. The ligature is left long to act as a guide. The vein is partly cut through just above the ligature and two of the small tenacula are hooked into the edges of the cross slit. The vessel is then completely divided and the third hook so placed as to expose its lumen.

It is important to keep control of the vessel with the hooks in this way, for the lumen is very hard to find if such a delicate vein is allowed to collapse.

The vein is gently dilated with a small hemostat. An infant's vein is fortunately much tougher than a cat's, and a very small vessel can be dilated to a useful size. After washing out the vein with salt solution, the tube, lubricated with vaselin, is inserted and secured with a fine silk ligature.

The donor's artery is clamped, divided and tied over the other end of the tube. One should make certain that the vein is not twisted before the tube is tied into the artery. When the clamp on the artery is removed, the stream of blood is seen to start through the glass tube, but its continued flow can only be verified by the pulsations in the vein and the appearance of the child. An infant is very quickly filled with blood from an adult's radial, and careful watch should be kept of the baby's face to see that the blood is not transfused too rapidly or in too great an amount. In the second case here reported, the child's face became a little dusky at the end of five minutes but regained a normal, red color a few minutes after the transfusion was finished.

CASE REPORTS

CASE 1.—The first case, one of hemorrhage after a minor operation, was transfused by this method before the laboratory experiments had been completed. William L., an infant aged 6 months, weighing 11 pounds, entered the Boston Floating Hospital July 10, 1910, on account of intestinal indigestion. The next day an indurated mass was noticed in the child's right cheek. During the following twenty-four hours the induration increased and an ulcerated area appeared on the buccal surface of the cheek. July 13, an incision was made into the cheek but no pus was found. After the operation, there was a small but persistent hemorrhage from the wound which continued throughout the night. Several dressings were soaked with blood. In the morning the bleeding not having checked, the child was sent to the Boston Children's Hospital. As far as could be learned, the baby had never bled in this way before, nor was there any suggestion of hemophilia in the family history.

When examined in the Children's Hospital, the child was still losing a little thin, watery blood from a 2-inch incision in the right cheek. The wound was sutured and the oozing stopped. The infant, however, was in poor condition. The skin, lips, and fingers were blanched. The respirations were rapid and shallow, and the pulse, though perceptible, could not be counted at the wrist. The hands and feet were cold. The child was semi-conscious. Preparations were at once made for transfusion. Unfortunately, in the hurry, the hemoglobin and coagulation time were not determined.

The mother, a small woman, served as donor. Her right radial artery was exposed under cocaine. The vessel proved to be unusually small. It scarcely seemed half the normal size. The child required little ether. An incision was made over the long saphenous vein at about the middle of the right thigh. The superficial vein not being found after a short search, the dissection was carried down to the femoral vein above Hunter's canal. The vessel was isolated for about an inch of its length and connected with the donor's artery by means of a coated glass tube, in the manner already described. In this case the tube was not filled with salt solution, but the air which passed into the infant's circulation

apparently did no harm. The tube was 6 cm. in length and 2.5 mm. in diameter. The flow of blood lasted for about seven minutes. When disconnected at the end of ten minutes, the tube was filled with a clot. In that time the child's color had greatly improved. Lips, ears and fingers showed a red tinge. The breathing was slower and deeper and the pulse stronger and fuller at the wrist. After ligating the femoral vein the lower leg became swollen and slightly blue. This passed away in a few hours. One hour after the operation, the child's pulse had fallen to 140. The improved condition, which immediately followed the operation, was maintained during the day and succeeding night. From this point the convalescence was uneventful and the infant was referred back to the Floating Hospital ten days after the transfusion.

CASE 2.—The second case was one of hemorrhagic disease of the new-born. James S., was referred to the Infant's Hospital in Boston by Dr. Homan of Everett, Mass., Oct. 11, 1910. The child, born two days before, at full term, normal delivery, was perfectly well up to 1 a. m. on the day of entrance, when he began to vomit blood in large clots. He vomited frequently and spat up bright, red blood after each feeding. During the day he had three movements containing red blood. He was brought to the hospital at 4 p. m.

The child weighed $6\frac{1}{2}$ pounds. The skin was slightly jaundiced and very pale. There was still a trace of color in the lips. About the mouth and anus, the skin was stained with fresh blood. There were several small points of subcutaneous hemorrhages on the upper lip and in the groin. Heart, lungs and abdomen were negative. The umbilical cord was normal. The pulse could be felt at the wrist, but was too rapid to count accurately.

The infant had evidently lost considerable blood, enough to seriously affect his condition, and was in a poor state to resist any further hemorrhage. For this reason it seemed best not to temporize with the less radical measures, but to proceed, as soon as possible, with a transfusion which would stop the bleeding and, at the same time, restore the cellular elements of the blood. The father of the child served as donor. While awaiting his arrival, and preparing for the operation, the infant vomited blood twice and passed another bloody stool.

The father's left radial artery was exposed under cocain in the usual manner. The child was then given a little ether and its femoral vein isolated for about one inch in the middle of the thigh. The vein was collapsed, and, in this state, seemed scarcely more than one millimeter in diameter. Considerable difficulty was experienced in exposing the lumen of such a small vein, but once the three hooks were in place, it was possible to dilate it enough to admit the tube. Following the technic already described, the vessels of the donor and recipient were connected with a coated glass tube 8 cm. long and 3 mm. in diameter. In this case the entrance of air was obviated by using a tube filled with salt solution. The blood had been flowing for about one minute when, by some mischance, the tube was pulled from the father's artery. Before it could be replaced, the blood had clotted in its lumen. The extra tube which had been prepared was then substituted and the blood allowed to flow for four minutes. The infant rapidly took on a healthy, red color. The face was becoming a trifle dusky when the transfusion was brought to an end. Counting the time the first tube was in use, the total flow must have been of about five minutes' duration.

The next day the patient was to all appearances a normal, healthy baby. There was no more bleeding. He vomited once after the first whey feeding. During the day he passed two dark movements. Three days after the transfusion the wound was clean and the infant was sent home to be nursed by the mother. A month later he was reported in perfect health.

CASE 3.—The third case was referred to the Infant's Hospital for hemorrhagic disease of the new-born Feb. 18, 1911. Chester P. was born four days before entrance, and for the first two days appeared to be a normal, healthy baby. On the third day he did not seem so well and passed a movement containing dark blood. The next day the baby had six black movements consisting, for the most

part, of clotted blood. He vomited once but the vomitus contained no blood. The bleeding from the bowel continued until the infant became too weak to nurse, and he had lost his healthy color when brought to the hospital at 1:30 p. m. on the fifth day.

When examined at 4 p. m. he was pale but not blanched. There was some color in the lips and fingers. He had a strong cry. Heart and lungs were negative. An odor from the umbilical dressing could be easily detected. The cord was moist and sloughing, but there was no redness or induration in the skin about the umbilicus. The temperature was subnormal. The pulse was 150 at the wrist, and the respirations were regular and not rapid. The hemoglobin was 35 per cent.

At 5 p. m. the baby had a large, dark movement with a suggestion of red color. At 6 p. m. there was another dark movement but no fresh blood. At 9 p. m. he had a small, dark movement with a little fresh blood.

The baby was given 10 c.c. of a thrombin solution, prepared by Dr. W. P. Lucas, at 11 p. m., and this was repeated twice the next morning. During the night the infant had a normal fecal movement but at 8 a. m. he passed another dark stool containing a little fresh blood. The morning temperature was 101.8 F.

At this time the baby's condition seemed as good or better than the day before, and it was decided to postpone transfusion, with the understanding that it should be done in the evening for any more bleeding, even if the infant's condition had not become worse.

The baby showed no change up to 1:30 p. m. when there was a sudden collapse. He lost all his color, the breathing became labored and the pulse was imperceptible at the wrist; hands and feet were cold. He passed a small movement of fresh blood. The father was summoned at once to serve as donor.

The operation began at 2:30 p. m. The father's left radial artery was exposed under cocain. The baby needed almost no ether. His femoral vein was isolated in the left thigh. The subcutaneous tissues were exsanguinated and the little blood which escaped from the deeper vessels was thin and watery. The coated tube used in this case was 12 cm. long and 3 mm. in diameter and this extra length made it easier to complete the connection with the donor's artery.

The father had a strong pulse and large radial, and the baby was filled with blood very rapidly. The connection was maintained for four minutes, and during this period the flow was checked three times, for a few seconds, when the infant's face became a little dusky. At the end of the operation the child began to struggle and cry vigorously. The hemoglobin, taken immediately after the transfusion, was 90 per cent.

The baby slept well during the night. He regurgitated his feeding once and had one dark movement. There was no sign of fresh bleeding. In the morning the temperature was 99.8 F. During the day he had two more dark movements. The second day after the operation the temperature was normal and the baby passed a normal, yellow movement. One week after the transfusion, the infant was taking his feedings well. He had a good color and normal temperature.

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PROGRESS IN PEDIATRICS

BACTERIOLOGY AND PATHOLOGY

Allergy

(C. E. von Pirquet: *Arch. Int. Med.*, vii, 259)

"Allergy" is explained by von Pirquet as being the altered reaction of an organism, which has passed through a certain disease or intoxication, to subsequent attacks of the same bacteria or toxins; that is, a reaction which differs from the reaction to the first attack in time, quantity or quality. As a simple example, he cites the phenomena shown by a person when revaccinated, in distinction to the train of symptoms following a first vaccination. In the latter case, after an incubation period of eight or nine days, a papule forms which increases and goes through the stages of vesicle, pustule, crust and scar; while in the case of a revaccination a papule forms within twenty-four hours, and then soon subsides. Here there is a second reaction which differs as to time, quantity and quality from the first reaction and is a typical example of allergy.

Included within the term allergy also are the reaction after vaccination in the cutaneous tuberculin test of von Pirquet, and the local and general reactions after the subcutaneous injection of toxins (for example tuberculin), amounting in some cases to the very severe general reaction, collapse and death known as evidences of "anaphylaxis." Von Pirquet thus tabulates the divisions of allergy:

I. Altered reactivity according to time, compared to a first reaction after eight to twelve days. 1. Early reaction (immediate) within twenty-four hours. This can be obtained by: (a) Intravenous injection associated with general symptoms (death); (b) subcutaneous injection; here we have to distinguish: (1) General symptoms (fever, exanthema), (2) local symptoms (*Stichreaktion*), (3) co-reaction of other foci; (c) cutaneous vaccination; (d) conjunctival application. 2. Torpid early reaction—second to fourth day. 3. Accelerated reaction—fourth to seventh day.

II. Altered reactivity according to quantity. 1. Re-enforced reactivity (hyper-sensibility, a paradoxical reaction, anaphylaxis). 2. Lessened reactivity (hypersensibility). 3. Abolished reactivity (immunity).

III. Reactivity altered according to quality (changes regarding color, microscopic observations, etc.).

In this article he attempts to review all the evidences of allergy so far observed in all the different diseases and intoxications.

1. Serum Disease: The normal symptoms of "serum disease," arising after the injection of certain sera, as horse serum, in diphtheria antitoxin, are these: after an incubation period of eight to twelve days there occur fever, urticaria and joint pains. On a second injection allergic phenomena are very common; there is often an immediate reaction, that is within twenty-four hours or less; this may be local or may be very severe or even fatal in cases of anaphylaxis. There is then a change in the reaction as to time, quantity and quality. The phenomena in experimental serum disease in animals, are:

(1) Almost universal anaphylaxis caused by some sera in animals of another species—as horse serum in guinea-pigs. (2) Lessened susceptibility or anergy, or antianaphylaxis. (3) Specificity of serum allergy. (4) Passive anaphylaxis—that is, the transmission by the serum of allergic animals of the same susceptibility to another animal. (5) Transmission of allergy to offspring through the mother, not through the father. (6) Active allergy in the newly born, that is, the inability to cause anaphylaxis in newly born animals, which is parallel to the observed fact that serum disease is rare in human nurslings.

2. The injection of other albuminous substances, such as hemoglobin, egg albumin, extract of peas, etc., also give evidences of allergy; in especial, anaphylaxis has been noticed in connection with all these substances.

3. Urticaria and hay-fever, von Pirquet believes, are examples of allergy to specific toxins.

4. Vaccinia: The evidences of allergy in regard to revaccination have already been recounted.

5. In glanders, actinomycosis, lepra, diphtheria and the diseases caused by hyphomycetes, evidences of the different varieties of allergy are recorded.

6. In syphilis there is no present evidence of allergy, but von Pirquet believes that it is possible that as soon as a pure culture of the specific organism can be procured and the toxin extracted, that local allergic phenomena can be elicited; i. e., that a cutaneous test can be elicited similar to that for tuberculosis.

7. Tuberculosis is the disease in which allergy has been most widely studied on account of the diagnostic importance of the changed reactions. Von Pirquet reviews the different forms of allergy observed in tuberculosis:

1. The general reaction on subcutaneous or intravenous injection of tuberculin in tuberculous patients. If the dose is large enough the symptoms may be fatal. If the dose is smaller general symptoms of malaise and fever are present; also there is the focus reaction or the inflammatory symptoms in the neighborhood of tuberculous tissue.

2. Subcutaneous reaction or *Stichreaktion*; that is, a subcutaneous inflammation at the site of injection. This, he says, has been proved to be the most delicate test of allergy, and is generally positive in tuberculous children with doses of .10 mg. of tuberculin or less.

3. Local reactions; as, 1. Cutaneous reaction on vaccination (von Pirquet), which he says is not delicate. 2. Morro's percutaneous reaction. 3. Application to the mucous membranes, as to the conjunctiva in Calmette's reaction; or to the nasal mucous membrane.

The time necessary between the first infection and the development of allergy in tuberculosis von Pirquet thinks is one to three months.

A lessened susceptibility of tubercular individuals to tuberculin or "anergy" occurs, (1) in the first stage of infection, often in nurslings; in them the antibody has not had time to develop; (2) in the final stage of miliary tuberculosis; (3) in cachexia; (4) during measles; (5) during continued treatment with tuberculin; (6) a long time after the onset of tuberculosis; (7) in certain cases of idiosyncrasy.

In the discussion as to the cause of the phenomena of allergy von Pirquet says that he early observed an incongruity between them and the generally accepted theories as to the incubation period of disease. It was formerly taught that the incubation period in an infectious disease is due to the length of time necessary for the development of the microorganisms. On this basis how can the immediate reaction taking place on a second entrance of the organisms or their toxins be explained, he asks. The theory of von Pirquet is as follows: After the introduction into the organism of bacteria or toxins the body forms certain substances called antibodies, the time necessary for the development of which corresponds to the incubation period of the disease; these antibodies then combine with the products of the infecting agent, or with the toxin, in a biochemical reaction, the result of which is another toxin which is the direct cause of the symptoms of the disease, such as fever, exanthema, etc. In diseases such as variola, measles and chicken-pox, all having a similar incubation period, he believes the exanthem is not caused by the specific microorganism, but by the toxic digestion product produced by the interaction of the antibody with some product of the microorganism. If the bacteria or toxins are introduced again within a limited time, the antibody is still present, the reaction is immediate, the toxic substance results and the symptoms of allergy occur.

G. L. MEIGS.

METABOLISM AND NUTRITION

The Body of the Cretin

(A. Flinker: *Wien. klin. Wchnschr.*, 1911, *xxiv*, 6, p. 196)

Flinker compares the body of a cretin with that of a normal man of the same age and concludes that the cretin has a relatively large head, short neck, long trunk and very short legs, conditions also found during childhood. Development in the cretin has evidently progressed only as far as ordinarily occurs in children, which condition has been confirmed by many pathologic examinations.

MAURICE OSTHEIMER.

Infant Mortality

(S. W. Newmayer: *Pediatrics*, *xxiii*, No. 2)

Among other points Newmayer brings out the value of individual feeding according to the infant and not according to age, as shown by the history of a large institution for children in Philadelphia. In 1909, this institution fed all the infants, according to age, on a series of set formulas of milk mixtures, and the children were cared for by nursery maids. In June, 1909, this institution, based on the number of sick children, had about 65 per cent. of deaths, in July, 1909, about 55 per cent., and a similar death-rate for August. In 1910, the managers employed a physician who was well trained in diseases of children and infant feeding; they also substituted trained nurses for the nursery help. Each child was carefully examined and watched and fed according to the physician's advice. The results were, for June, 1910, 14 per cent. mortality; July 8 per cent., and for August but 4.4 per cent.

HENRY F. KEEVER.

Calcium Metabolism in a Case of Infantile Tetany

(H. D. Haskins and H. J. Gerstenberger, *Jour. Exper. Med.*, *xiii*, No. 3)

The authors report their experiments on calcium metabolism in an infant of 14 months suffering from tetany. Their observations embrace two periods, the first during the stage of active symptoms, covering a period of about six weeks; the second during the latent stage, covering one week. A table is given recording the amount of calcium in the food, the amount of calcium lactate administered, and the amount excreted in the urine and feces. Calcium lactate was given during only three weeks of the first period. The diet during the first series of experiments consisted of 100 c.c. of milk diluted with 100 c.c. of water; during the second series 1,000 c.c. of milk daily. Their results were as follows: the urinary calcium was slightly increased while calcium lactate was administered; calcium administration did not increase calcium retention; and there was no improvement in the symptoms during the administration of calcium lactate.

F. H. BARTLETT.

Should Eclamptic Mothers Nurse Their New-Born?

(J. R. Goodall: *Arch. Pediat.*, January, 1911, *xxviii*, No. 1)

Goodall, discussing the question from the standpoint of the child's interests, cites three instances occurring in his practice of babies dying without apparent cause in a few hours after the first appearance of milk in the mothers' breasts. The symptoms and manner of death in all three were identical—general depression, going into coma, cyanosis, convulsions, respiratory paralysis, slow, full pulse, and abdominal distention. The mothers were eclamptic, the children apparently normal at birth. The onset of the above symptoms followed in a few hours the first ingestion of the mothers' milk. Somewhat detailed reference is made to the literature on the subject to prove that the child of an eclamptic mother is never healthy at birth and that the lesions are identical with those of the mother. These children come into the world with their organs

generally diseased, especially the kidneys. Observations by Dienst are quoted as showing that all children born of eclamptic mothers give evidences of hepatic or renal lesions to a varying extent. The author considers maternal eclampsia a frequent source of chronic nephritis in young children, believing that the milk is more toxic than either the blood or urine, and that this toxicity varies with the persistence or non-persistence of the toxemia up to the time of the filling of the breasts with milk. He concludes that in toxic and jaundiced women maternal feeding should be delayed until the condition has been controlled, and that the persistence of albuminuria makes permanent artificial feeding necessary.

F. C. Z.

ACUTE INFECTIOUS DISEASES

Some of the Rarer Occurrences in the Rheumatism of Children

(F. J. Poynton: *Brit. Med. Jour.*, January 7, 1911)

Rashes. In an observation of 600 cases, Poynton saw forty rashes. They are usually urticarias and erythemata which may be mistaken for scarlet fever or ringworm. Psoriasis may alternate with chorea; this occurred four times in Poynton's series. Purpura and, rarely, a pemphigoid or bullous eruption may be observed. Finally, herpes has been observed independent of arsenic administration.

Erythema nodosum was observed fourteen times and it is asserted by Poynton that it is possibly not a manifestation of rheumatism, for heart disease is an unusual complication.

Venous thrombosis of the large veins in severe cases occurred five times. Localized edema, with subsequent discovery of the thrombosed veins, are diagnostic. Facial edema is occasionally caused in this way.

Tachycardia may be paroxysmal in onset and character. It is associated with mitral stenosis more frequently than with other lesions. It may precede the evident valvular lesion. In some of these cases the recovery is complete. If mitral stenosis develops, however, the tendency is for a rapid heart action to persist. As a rule Poynton has found no involvement of the thyroid and none of his cases have developed exophthalmic goiter.

Mastitis, as evidenced by slight enlargement and tenderness of the breasts in girls, was also observed by Still.

Epistaxis has been observed at the onset, during the illness or during the quiescent period. Hematemesis has been observed with grave heart disease.

J. G. M. BULLOWA.

Serum Treatment of Pneumonia in Children

(E. M. Sill: *Med. Rec.*, New York, 1911, *xxix*, 712)

About a year ago Sill became interested in a polyvalent, composite serum obtained from diphtheria-immune horses, for use in pneumonia. The serum was injected subcutaneously in doses of 10 c.c., at varying intervals, depending on the symptoms and the effect it had on the patient. In some cases one injection seemed to be sufficient to relieve the symptoms and check the disease, while in others repeated injections of 10 c.c. were given every day or at longer intervals, although not always with favorable results. Sill thinks that perhaps, in these latter cases, if large doses had been given or the serum had been injected at more frequent intervals, it might have made a difference and given a more immediately favorable result. In all, twelve patients were treated by means of the serum, eight males and four females. Their ages ranged from 5 months to 3 years; all but two were under 2 years, and three of these were under 1 year. There were three cases of lobar pneumonia and nine cases of bronchopneumonia. Two patients

died, one of empyema and one of extensive double pneumonia, marasmus and cardiac failure. (Mortality 16.6 per cent.). Two other patients besides those that died were not helped by the serum, but the other eight patients were all more or less improved and in some of the patients the effect of the serum seemed marked. Those patients who received serum early in the disease seemed to be most benefited by its use. This serum should be made in a concentrated form to prevent serum sickness, which has previously been the drawback to the animal serums. The polyvalent, composite serum, while it has not given brilliant results in all cases, is at least an advance in therapeutics in the right direction and apparently in a number of cases limited the disease. To obtain the best results from the serum treatment of pneumonias of mixed infection, the serum should be obtained from horses, not only immunized to the pneumococcus, but also to the other germs which are commonly found to be present in these cases. It is important that in pneumonia the child be injected early in the disease with good sized doses of a concentrated serum.

F. C. Z.

Diseases of the Cow in Their Relationship to Human Diseases

(W. G. Savage: *Proc. Roy. Soc. Med.*, March, 1911)

The part which the cow plays as a source of disease in man through the milk supply is studied by Savage under three heads: 1. General systemic disease of the cow without local lesion of the milk organs. 2. General systemic disease of the cow with local lesions in or on the udder and teats. 3. Local affections with little or no general systemic disturbance. Tuberculosis is excluded in this study. The danger from anthrax is a remote one, as the cow usually dies within a few hours after infection, though the bacillus has been recovered from the milk. Widespread outbreaks of food-poisoning have resulted from the consumption of meat infected with the Gaertner bacillus. In cows affected with diarrhea and other symptoms of gastro-enteritis the milk is usually abnormal and decomposes rapidly, and may produce diarrhea. In septic conditions, puerperal septicemia, metritis, etc., the milk is usually markedly altered and no doubt would be prejudicial. Cows are susceptible to Malta fever and the *Micrococcus melitensis* has been found in the milk. Though not mentioned by Savage it also affects goats and is recognized in Malta as the source of Mediterranean fever. In the second group, with local lesions of the teat and udder, are foot and mouth disease and cow-pox, the former of which may be transmitted to man through the milk as attested by a number of cases and outbreaks of the disease. The milkers' hands are likely to be infected with cow-pox, but there is little evidence of the harmfulness of the milk. The most interesting group is the third in which the essential lesions are in connection with the milk-producing organs. They take the form of mastitis and the various conditions described as ulcerated teats. Epidemics of illness ascribed to mastitis have nearly always been of the nature of septic sore throat, although there are one or two in which gastro-enteritis has been the predominant condition, of which Holst records four epidemics in which the organism was the mastitis streptococci. Savage records a large number of outbreaks of this nature extending over a considerable period of time, in some of which several hundred cases were reported. To determine whether the streptococci found in cow mastitis were pathogenic to man Savage conducted some investigations in sixteen cases of human sore throat. Two chief types were found, confirming the results previously found by Andrewes and Horder, the most prevalent type being the variety which they called *Streptococcus anginosus*, while the other was identical with the *S. pyogenes*. Further experiments by Savage led him to the conclusion that the great majority of cases of bovine mastitis are due to an organism not pathogenic to man, but that in certain uncommon cases this condition is caused by a streptococci highly pathogenic to man. The pathogenic and the non-pathogenic types, however, are not clinically distinguishable. If ulcerated teats have

any relationship to human disease Savage believes it may be accounted for in three ways—the ulceration may be part of a general disease of the cow, and through the teat ulcerations the milk may become infected; the teat and udder conditions may be purely local, but due to streptococci or other organisms pathogenic to man; the teat conditions may be due to purely bovine disease, but become secondarily infected by organisms pathogenic to man; in other words, we may have a constitutionally infective cow, a local actively infective cow, and a local passively infective cow. In addition to streptococcal infection, teat lesions may be secondarily infected with diphtheria bacilli, and Savage reports a number of epidemics from this source. As to scarlet fever, Savage believes that the existence of a constitutional disease, bovine scarlet fever, cannot be accepted as proved; but as an explanation of the extensive outbreaks of scarlet fever clearly traceable to milk as at Hendon in 1885 and in certain parts of London and Surrey in 1909, Savage suggests the hypothesis that when the cow is the source of scarlet fever, or other septic disease, it is because it is acting as the carrier of organisms of human origin, often in a purely passive capacity.

J. B. C.

Hemorrhagic Disease of the Newborn

(R. M. Green and J. B. Swift: *Boston Med. and Surg. Jour.*, 1911, *clxiv*, 454)

The fifty-one cases which form the basis of this paper occurred in the wards of the Boston Lying-In Hospital from June 19, 1904, to April 1, 1910, a period of nearly six years. The total number of babies born in the hospital during this time was 4,455, showing a percentage incidence of 1.14 per cent. as against 0.57 per cent. in Townsend's series. Of the fifty-one mothers, thirty-one were primiparæ, twenty were multiparæ. In none of the multiparæ of this series is there any record of hemorrhage in previous children. This fact would tend to controvert the theory that the disease is analogous to hemophilia, or in any way dependent on a hereditary dyscrasia. Thirteen of the fifty-one mothers were single, thirty-eight were married. The presentation of the fetus in every case was a vertex. The longest labor of the series ran to seventy hours, but this baby recovered, and of the twenty-five who died, ten were born after less than twelve hours of labor. The average duration of labor for the entire series is fourteen hours thirty-seven minutes, which is only slightly above the general average for a large number of unselected cases. Nine of the labors were forceps deliveries, again about the same percentage as of all cases in the clinic. One of the mothers had pneumonia at the time of delivery, one had mitral regurgitation, and one impending eclampsia. One mother was an epileptic. Three of the puerperia were complicated by slight uterine sepsis, two by mastitis, one by salpingitis, and one by scarlet fever. It does not seem that any of these complications or attendant circumstances could have had any bearing on the hemorrhagic condition. Of the fifty-one cases, thirty-nine occurred during the six months from November to April, inclusive, and only twelve during the six months from May to October, inclusive. This proportion, which is essentially the same as that of the seasonal incidence of such infections as impetigo, diphtheria and bronchopneumonia, the authors think, should confirm the theory of the infectious etiology of the disease, which is more prevalent during the months when ventilation is poorest and general resistance to infection is lowered. Again it is instructive to observe that thirty-three of the cases occurred in distinct groups, after the manner of hospital infections. The average age at onset for the entire series was $3\frac{1}{2}$ days. The average age at onset for the fatal cases was only slightly less, $3\frac{1}{5}$ days. The only two cases that began after the tenth day resulted in recovery. The greatest age at onset among the fatal cases was 9 days, but all the other fatal cases occurred under 7 days. This would seem to indicate that after ten days the disease is infrequent and the prognosis good; that after a week, the prognosis is fairly good; but that under a week the prognosis is poor and the age at onset has no particular bearing on the prognosis. Clinically the cases arrange themselves in

three distinct groups as follows: First, those in which the hemorrhage is principally from the umbilicus; second, those in which it is principally from the mucous or serous membranes; third, those characterized principally by the formation of subcutaneous purpuric patches or ecchymoses. These types the authors designate, respectively, the umbilical, the seromucous and the purpuric, according to which form of hemorrhage predominates. The important bearing of this classification is on prognosis. The mortality of the umbilical type is about 60 per cent., that of the sero-mucous type about 50 per cent., and that of the purpuric type about 22 per cent. The treatment of these patients was supportive, hemostatic and by means of normal rabbit serum, which was given subcutaneously in 30 c.c. doses, repeated two or three times, in case the bleeding recurred after the first dose. The results of treatment are tabulated as follows:

Treatment	Recoveries	Deaths	Total
General Supportive	2	4	6
Local hemostatic	2	5	7
Gelatin	9	4	13
Rabbit serum	12	10	22
None	1	2	3
	26	25	51

Crile's experiments in direct blood transfusion suggested its use in one case, after a dose of rabbit serum had failed to arrest bleeding. The transfusion was successful, but the patient died. F. C. Z.

TUBERCULOSIS AND SYPHILIS

Treatment of Congenital Lues in Infants, by Injecting Salvarsan ("606") Into the Nursing Mother.

(K. Taege: *München. med. Wchnschr.*, 1910, lvii, No. 33; R. Duhot: *ibid* No. 35; M. Dobrovitz: *Wien med. Wchnschr.*, 1910, No. 38; J. E. R. McDonagh: *Brit. Jour. Child. Dis.*, October, 1910; Meirowsky and Hartmann: *Med. Klin., Berlin*, 1910, vi, No. 40; P. Ehrlich: *Deutsch. med. Wchnschr.*, 1910, No. 41; J. Peiser: *Berl. klin. Wchnschr.*, 1910, xlvii, No. 1.)

Taege was treating a luetic mother in the Freiburg Klinik, and ten days post-partum injected 0.3 gm. of salvarsan into the mother. The infant had shown specific symptoms for two days, and for two days more the symptoms progressed; on the third day a cessation was noticed, and by the fifth there was a complete change for the better. Examination of the mother's milk for arsenic was negative.

In Duhot's case a child in a very serious condition was rescued from almost certain death by the salvarsan treatment ("accidentally") given its mother. The child had no mercurial treatment and was certainly benefited after the injection of the mother. He concludes that a luetic woman treated with salvarsan is the best wet-nurse for a luetic child whose mother can not nurse it.

Dobrovitz had one case, the four months' old child of a mother who denied lues; it showed soon after birth a pustular eruption which gradually spread, and showed other clear signs of lues. The mother showed no clinical signs, but the Wassermann reaction was positive; she was nursing the child, and received one injection of salvarsan. Four days later many of the lesions on the child's skin healed. It is to be noted that in spite of the febrile and other constitutional symptoms exhibited by the mother, for three days after injection the milk secretion was not affected and the child was remarkably quiet.

Meirowsky and Hartmann, instigated by the reports of Taege and Duhot, tried the plan of treating a congenitally luetic infant with the blood-serum of a patient

treated with salvarsan. The mother showed only the typical ulcerated papules on the genitalia, and was delivered of a male child apparently healthy; during the first two weeks it showed no symptoms; then came a typical efflorescence on the palms, soles and buttocks, and later on more symptoms. Since the nursing period of the mother was ended, the child was treated with the blood-serum of a patient treated with salvarsan; two days after the first injection came the first signs of change, the soles of the feet becoming clear; after seven more injections very few symptoms were left, although three days later a coryza and a periostitis of the arm were present. While no complete cure is claimed here, an improvement certainly followed, and the authors believe they would have had better results with larger doses of serum.

Peiser tried this treatment in two cases in the clinic of Dr. Ritter in Berlin; the first case had visceral lues, manifest from birth, and evidently fetal; general condition poor, prognosis doubtful. The second patient showed luetic symptoms only a few days after birth, which were confined mostly to skin and mucous membrane; general condition good, prognosis good. The results in both cases were negative, and both infants died; at first all symptoms disappeared, but they soon came again, more severely, and apparently opened the way for a secondary infection. Wassermann reaction was positive in both mothers before the injection of salvarsan; it was absent in the mother of the first case after the death of the infant. The other mother went away before she could be retested.

Ehrlich, in a general discussion of the formation of antibodies after the injection of salvarsan, includes a consideration of the reports of Taege and Duhot, and says that since arsenic was not found at all or at most in minute quantities in the milk of these women treated with salvarsan, and since salvarsan used *per os* even in large doses has but little effect, the possible factor of antibodies must be considered, the sudden death of so many spirochetes having set free a large amount of endotoxins, which went with the milk. This is perhaps analogous to the *säuglings immunität* already described; additional evidence is offered in the fact that the blood-serum of patients treated with salvarsan has a curative effect on new-born luetic children, as reported by Marinesco, Plaut, Scholtz, and L. Michaelis. This latter method is certainly better than the direct one on the child, which may cause severe nutritional disturbances, due probably to the sudden production of endotoxins in the blood, after the sudden dissolution of the spirochetes.

McDonagh refers to the cases of Taege and Duhot, and remarks that if merely injecting the mother is going to cure the child, the latter need not be injected; thereby the risk of poisoning from an overdose is obviated; but one must bear in mind the possibility of a recurrence, if treating the mother is solely relied on, as one can scarcely believe that the amount of antitoxin absorbed from the milk would be as potent as an injection.

A. C. SOPER, JR.

Salvarsan Treatment of Infants

(A. Doblin: *Berl. klin. Wehnschr.*, 1911, No. 12)

Doblin treated six infants directly with salvarsan, subcutaneously or intramuscularly. Two were apparently hopeless from the beginning and showed absolutely no improvement. The other four were at the time of the injections in a tolerable condition, and exhibited the varying symptoms of pallor, rhinitis, dermatitis exfoliativa, visceral lues, roseola, or glandular swelling. In contradistinction to the effect on adults, none of these showed a strong necrotic area at the site of the injection, during an observation of over three weeks; only a hard swelling appeared, which neither became red nor ulcerated. On the luetic symptoms the influence was marked, especially on the skin, but least on the rhinitis and glandular swellings. As to the viscera, not enough time elapsed to be certain; of the two cases brought to autopsy, no spirochetes were found in the liver.

No claim is made of an influence for the better as regards the general condition; three months later one patient was still in a very weak condition; one

infant died in a month, of erysipelas; one patient, seen first in a collapse, died one day later; one, very sick, but in no way moribund, died one day later; one child in good condition from the first, still showed adenopathy five weeks later.

No patient, then, could be considered as benefited to any great extent; generally the pallor persisted throughout, and the weight curve did not rise to any extent.

A. C. SOPER, JR.

RESPIRATORY SYSTEM

Acute Adenoiditis

(*Felix Schleissner: Wien. klin. Wchnschr., 1911, xxiv, 9, p. 310*)

Schleissner discusses acute inflammation of the postnasal adenoid tissue in children, which is generally accompanied by cervical adenitis and fever, the cervical adenitis or glandular fever being secondary to the adenoiditis. He considers acute adenoiditis a better name for this condition than glandular fever. The condition is not only found in children of all ages, but even occurs in infants under one year of age. While it is not easy to make the diagnosis on the first day of illness, it is not difficult in a few days, though retropharyngeal abscess may be simulated in young children. Usually every symptom, except the enlarged glands, clears up in a few days. The cause is undoubtedly an infection. The glandular swelling gradually disappears spontaneously.

MAURICE OSTHEIMER.

When Shall We Remove Tonsils and What Type of Operation Shall We Do?

(*E. A. Crockett: Boston Med. and Surg. Jour., 1911, cxlv, 414*)

The author believes that in unskilled hands the operation for removal of tonsils will show a higher mortality than an abdominal section for the removal of the appendix after recovery from an acute attack in the hands of a good surgeon, and therefore it is not wise to advise such removal except for sufficient symptoms. In children one should remove the tonsils (1) in all cases in which the child presents large, non-adherent tonsils, largely filling the cavity of the pharynx; (2) in all cases which are associated with enlarged glands in the neck and in all cases of articular rheumatism in which the tonsil is probably an etiologic factor. These operations should be performed, as a rule, in the quiescent period. Endocarditis, in a more or less chronic state, need not necessarily be regarded as a contra-indication for operation. (3) The tonsils should be enucleated in all cases of repeated peritonsillar abscess. Tonsils should not be removed (1) when they are of moderate size, i. e., projecting not over a quarter of an inch beyond the anterior and posterior pillars; (2) under the promise to the parents that their removal will relieve the child of cold in the head or ear trouble. In adults tonsils which are distinctly pathologic, but which give no symptom at present, though they may have caused trouble in childhood, should not be removed. With this exception indications for operation are the same in adults as in children. The mere fact that a child is under ether for an adenoid operation should not be considered justification for the removal of tonsils.

If the case presents a clear history of infection—peritonsillar abscess, acute articular rheumatism, tubercular infection of the neck—the whole tonsil should be enucleated and removed as completely as possible. This should be done by blunt dissection. In an ordinary case of simple hypertrophy devoid of symptoms, the most common type in children, a perfect result may be obtained by removing enough of the tonsil to bring it down to normal size.

From a consideration of accidents which have followed enucleation of the tonsils, Crockett believes that an operation in the throat requiring the use of general anesthesia is too dangerous a procedure for any one to perform, who is

not thoroughly competent to meet the surgical emergencies which may occur. These comprise ability to ligate the common carotid, to ligate the tonsil pillars, to do an emergency tracheotomy, and to perform artificial respiration.

RICHARD M. SMITH.

BLOOD AND CIRCULATORY SYSTEM

Venous Murmurs at the Root of the Neck in Children

(Carey Coombs: *Brit. Jour. Child. Dis.*, 1911, viii, 109)

In a majority of children varying in age from 3 to 15 years, Coombs heard a murmur immediately below the sternoclavicular joint or joints. It was slightly commoner in boys. It was commoner and louder on the right side. This murmur is continuous, but accentuated at the beginning of systole and of diastole, especially the latter. It is at its loudest during the inspiration. Though often heard with the head in the erect position, it was in such cases heard more clearly, and in some other cases heard only, when the head was fully retracted. Lateral rotation of the head also makes it more clearly audible. It is usually abolished when the patient lies down. It is produced in the internal jugular veins; by what mechanism is not clear to Coombs, though its accentuation by retraction of the head is no doubt due to flattening of the veins against the transverse processes of the cervical spine. Though associated with anemia and febrile states, it is heard also in perfectly healthy children. It is not specially associated with tuberculosis or any enlargement of the intrathoracic lymph-glands, and has no diagnostic value.

F. C. ZAPFFE.

Effect of Exercise on Systolic, Diastolic and Pulse Pressures and Pulse Rate.

(O. S. Lowsley: *Am. Jour. Physiol.*, 1911, xxvii, 446)

All types of prolonged exercise which cause an increase in pulse rate cause also a rise in systolic and diastolic pressures. The systolic pressure shows the greater rise, hence there is an increase in pulse pressure which may be interpreted to mean that the heart beats are augmented as well as accelerated. After all types of exercise which were studied, the systolic, diastolic and pulse pressures invariably fall below normal and remain in this subnormal condition for a considerable time. The more exhaustive the nature of the exercise the longer will be the subnormal period which follows. Systolic pressure invariably falls more rapidly than diastolic and hence the pulse pressure becomes weaker. The presence of albumin in the urine coincident with low pressure was observed, just as in the cases reported by Erlanger and Hooker (*Johns Hopkins Hosp. Rep.*, 1904, xii, 145-378). This seems to add another factor to the possible injurious results of long continued exhaustive exercise. The pulse rate, which always increases during exercise, decreases rapidly after its completion. This drop in the curve of the pulse rate is frequently followed by a secondary rise, which is possibly a reflex effect due to the low blood pressure of the subnormal stage. In no case was this secondary rise in pulse rate accompanied by a rise in blood pressure. Vigorous, fatiguing and exhausting exercise is followed by a subnormal blood-pressure, which lasts the longer the more severe the exercise. If the interpretation of these results is correct, the so-called field events, such as shot putting, discus and hammer throwing, jumping, baseball, and exercises of a similar nature are preferable for the rapidly growing youth, to basket ball, football and running races. There is less strain put on the circulatory system by walking a number of miles at a moderate rate than by sprinting 100 yards at top speed. Long distance running and similar forms of exhaustive exercise give rise to serious strain on the heart, as is indicated by the long period of subnormal blood pressure.

FRITZ B. TALBOT.

NERVOUS SYSTEM

The Prevention of Feeble-Mindedness

(*E. R. Johnson: Jour. Am. Pub. Health Assn., 1911, i, 90*)

From a study of cases in the Training School at Vineland, N. J., the author has compiled statistics of the occurrence of feeble-mindedness in families. In seventy-seven families there were 352 feeble-minded individuals. In the 113 families having relatives in the school, numbering 495, only 177 or 35.8 per cent. were normal. He urges a careful and painstaking collection of statistics to secure the facts on which to base further preventive action. He believes heredity plays a large part in the production of feeble-mindedness, so that the real point of attack is the feeble-minded person who would become a parent.

RICHARD M. SMITH.

GENITO-URINARY SYSTEM

Lordotic Albuminuria in School Children

(*L. Piesen: Wien. klin. Wchnschr., 1911, xxiv, 1, p. 12*)

Piesen has made a series of analyses of urine from school children, both before and after standing five minutes in lordosis; also before and after sitting in the ordinary school position with the arms crossed. In the former he found albumin in from 32 to 46 per cent. of the children; in the latter, in from 12 to 28 per cent. The age of the children was apparently not of any significance; the height of the children, on the other hand, was important, as most of the taller children developed albuminuria. The kidneys were not palpable in four-fifths of the children examined; while albuminuria was found in one-third of these, it also occurred in over half of those in whom the kidneys were palpable. Piesen concludes that the ordinary method of sitting, with the arms crossed, should be forbidden; that the taller the child, the greater is the tendency to lordotic albuminuria; that this disposition increases with age; and, finally, that statistical investigations show that lordotic albuminuria does not depend on movability of the kidneys.

MAURICE OSTHEIMER.

SKIN AND APPENDAGES

Alopecia Epidemic Due to the Microsporon

(*R. O. Stein: Wien. klin. Wchnschr., 1911, xxiv, 9, 308*)

Stein reports twelve cases of alopecia which he found to be due to the microsporon Audouini. All these cases occurred among the children attending one school in Vienna. The microsporon first attacks the skin situated near the margin of the scalp, as in the nape of the neck, about the ears, etc. Where or how the first child became infected was not discovered.

MAURICE OSTHEIMER.

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THE DIAGNOSIS OF INFANTILE TETANY

WITH A REPORT ON EXPERIMENTAL TETANY IN DOGS *

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NEW YORK

Tetany, in infants, has been recognized for many years as a disease entity evidenced by laryngospasm, respiratory spasm, muscular rigidity, contractures of the extremities, convulsions and even coma, and more recently by increased response to electrical and mechanical nervous stimulation. Many causes have been given for this symptom-complex, the earliest referring to tetany as the most dangerous of the complications associated with dentition. The first accurate description of the disease is that of J. Clark in 1815, which gives in detail the characteristic respiratory and muscular conditions. A few years later Marshall Hall wrote of the symptoms as brought about by stimulation of the central nervous system through peripheral irritation. In 1829 Kopp attributed the laryngospasm to thymus hypertrophy and at about the same time Leigh claimed that it was due to pressure on the vagus by enlarged tracheobronchial lymph-glands.

The first investigation of the electrical hyperirritability of children suffering from tetany was carried on by Escherich and von Wagener in 1890. In this and later communications¹ was established the fact that there is an increase of electrical irritability in all cases of the disease, and that this makes its appearance before the existence of muscular spasm and is demonstrable after the latter has disappeared.

A few years after this Thiemich² ascertained the normal electrical irritability in young children and stated that, of the variations from this evidenced by those having tetany, the most significant one was the appearance of anodal opening contraction at a point lower than anodal closure and that of kathodal opening contraction below 5 milliamperes of current strength.

* From the Children's Service of Bellevue Hospital, First Medical Division, New York City.

1. Escherich: *Die Tetanie der Kinder*, 1909.

2. Thiemich: *Ueber Tetanie und Tetanoide Zustände im Ersten Kindesalter*, *Jahrb. f. Kinderh.*, 1900, li.

The determination of the normal response to galvanic stimulation in children and the knowledge that this became greatly increased in tetany provided a more certain method of diagnosis than had previously been at hand. Its application to large numbers of children brought out the fact that tetany was much more frequent than had been before believed. Indeed, Finkelstein³ found that between 40 and 45 per cent. of artificially nourished children, on being subjected to the galvanic test, showed increased electrical irritability. His observations and those of Gregor, tending to show that electrical irritability was more marked in children fed on cow's-milk than in those on breast-milk or farinaceous foods, indicated that anomalous conditions of assimilation might produce electrical and, at times, other symptoms of tetany. This was attributed both to the greater calcium content of the cow's-milk and to the presence in this serum of an unknown substance which is lacking alike in breast-milk and in farinaceous foods.

Although it has been demonstrated that electrical response does vary with changes in digestive and metabolic processes, the fact remains that by this method of electrical tests, cases hitherto not suspected of tetany may be brought to correct diagnosis. Just what electrical findings are essential to a diagnosis of tetany has been and is still a matter of dispute. Thiemich's contention was that a kathodal opening contraction must be obtained at a point less than 5 milliamperes if tetany is to be proved. Ganghofner⁴ confirmed Thiemich's findings, but stated that in many unquestionable cases of tetany the kathodal opening never dropped below 5 milliamperes, and that, moreover, other children had distinct electrical hyperirritability who never before or after had shown any signs of having tetany. Von Pirquet⁵ decided from a large experience that the normal reactions of children were lower than Mann found them to be and that the appearance of anodal opening below 5 milliamperes was certain evidence of increased electrical irritability. Escherich believed that in normal children only kathodal closing contraction appears under 5 milliamperes and that only occasionally may anodal closure be present with this current strength.

My own study of the muscular response to galvanism is in two parts. The first, consisting of the routine testing of 118 infants in the children's ward of Bellevue Hospital, was instituted with the intention of adding our experience to the foregoing studies of the electrical response in children, normal in so far as their nervous systems were concerned; to deter-

3. Finkelstein: Zur Kenntniss der Tetanie und der Tetanoiden Zustände der Kinder, Fortschr. d. Med., 1902, No. 20.

4. Ganghofner: Zur diagnose der Tetanie im ersten Kindesalter, Ztschr. f. Heilk., 1901.

5. Von Pirquet: Die Anodische Uebererregbarkeit der Säuglingen, Wien. med. Presse, 1907, No. 1.

mine what percentage of such routine tests resulted in distinct evidence of hyperirritability, and, if possible, to follow those children showing such reactions to see if they ultimately did develop frank tetany.

It is very difficult to define exactly the normal electrical response of childhood. Some children react low one day and high the next. Some give low closing contractions for kathode and anode, others lower anodal opening than anodal closure. It is common to obtain kathodal closure response below 2 milliamperes, while the other reactions are well above 5 milliamperes. In view of the number of our children, normal as to their nervous systems, who in this series gave reactions other than kathodal closure below 5 milliamperes, and in view of our experience with the reactions of normal dogs, it seems that Escherich's definition of hyperirritability imposes rather too narrow limits on the normal reaction, but it is, nevertheless, followed as a basis of division in the following tables.

It is well understood that definite conclusions cannot always be drawn from such classifications and averages as are hereafter given. They are, however, valuable as teaching something of the results to be expected in electrical tests in infants apparently normal in so far as their nervous systems are concerned, and do not apply to those suspected of or actually suffering from tetany.

The second part of the article, dealing with the electrical reactions in dogs, is intended to demonstrate that in normal dogs these reactions are similar to those in normal children, and to offer some observations on the relation between lesions in the parathyroid glands and electrical hyperirritability as the first evidence of the ensuing tetany.

We have to consider, then, a disease rather common in infancy and also in adult life, but in the former case presenting an entirely different symptom-complex from that of the adult type.

Potpeschnigg found the incidence of tetany to be 109 unquestionable cases in 10,000 children observed in the Grazer children's clinic in 1900-1904, or about 1 per cent. The greatest number of cases occurred between the third and twentieth month, during this period going as high as from 4 to 6 per cent. of the children admitted between these ages. There is a wide divergence of opinion on the question of the frequency of the disease, due, presumably, to the varying attitudes of the observers as to what constitutes a true diagnosis. Various authors give figures varying from 6 per cent. down to 0.7 per cent. in artificially fed children under 3 years of age.

In Dr. Howland's service at Bellevue, of 934 children under 2 years admitted from October, 1909, to March, 1911, there were five unmistakable cases of tetany, or 0.5 per cent. Two of these were admitted before the routine electrical tests were begun and were not so tested. The three others showed marked hyperirritability to galvanism in addition to laryngo- and respiratory spasm and muscular rigidity.

The type of tetany generally presented by children of this age is that accompanied by great general irritability, laryngospasm and respiratory spasm, with or without convulsions, rather than by spasm of the extremities. The latter condition is, however, demonstrable in most cases if carefully sought for. The electrical diagnosis of tetany, the technic and details of which are later referred to, depends on the obtaining of muscular response to galvanic stimulation with kathodal and anodal closure and opening at a current strength of less than 5 milliamperes. Such electrical hyperirritability, that is, an irritability toward all four forms of current, is not present in children with normal nervous systems. It appears early in the course of tetany and, while varying greatly from time to time, persists after all other tetanoid symptoms are absent. An instance of the variation sometimes found is that of a 15 months' child who, on the first test, reacted to kathodal closure, 0.6 milliamperes; anodal closure, 1.6; anodal opening, 1.6; kathodal opening, 2.3. Six days later, kathodal closure, 2.0; anodal closure, 4.0; anodal opening, 3.0; kathodal opening greater than 5.0, and after three days gave in a third test: kathodal closure, 1.6; anodal closure, 3.0; anodal opening, 1.3; kathodal opening, 3.0.

An incomplete reaction may be frequent in cases of true tetany. This is shown in Dogs 3 and 6, neither of which gave response to kathodal opening below 5 milliamperes, although both unmistakably died of the disease. It is evident from this and other similar experience that a true decision for or against tetany can be reached only after repeated galvanic tests.

Escherich's investigation of children under 6 months of age showed 55 per cent. evidencing hyperirritability; i. e., giving some reactions other than kathodal closure with currents of less than 5 milliamperes.

In my series of 318 electrical tests, ten, or 3.1 per cent., gave evidence of extreme or kathodal hyperirritability. Of the middle grade or anodal irritability giving response to kathodal closure and anodal closure alone below 5 milliamperes, there were 101, or 31.8 per cent. With kathodal closure and anodal opening alone present, below 5 milliamperes, I found fifty, or 16.6 per cent. With both kathodal closure, anodal closure and anodal opening, less than 5 milliamperes, there were forty, or 12 per cent. The occurrence, then, in my series of abnormal reaction or increased electrical response according to Escherich's definition was 193, or 61 per cent.

Of these cases of anodal or partial hyperirritability, none developed other symptoms of tetany under observation. What then does this condition of partial irritability mean? Is it a state of exaggerated nervous sensitiveness quite unrelated to tetany and to be expected in about one-half of the children who come under observation? Is it an evidence of the past existence of the disease, or may it be the precursor of the devel-

opment of tetany in its true form? The first hypothesis would seem to be the most probable one, and if so, necessitates the definition of normal electrical reaction as a condition of irritability responding by muscular contraction to kathodal closure alone with currents of less than 5 milliamperes strength, or in an equal number of instances, to anodal closure and anodal opening stimulation with the same weak current, the former being twice as frequently found as the latter. Reason for this belief is found in the fact that the condition is common to so many children who evidently have not tetany, and strength is added to it by the demonstration of the same type of irritability on my dogs before operation.

On the other hand, and perhaps in support of the theory that this anodal irritability is the precursor of true tetany, it will be noted that in all the partially parathyroidectomized animals there was evident an increasing grade of anodal irritability. Further experiments bearing on this point are at present in progress.

Evidence of mechanical hyperirritability in tetany may be demonstrated in the following ways:

The Chvostek Sign.—This depends on reflex contractions produced in the muscles at the angle of the mouth, the ala of the nostril and brow by tapping the cheek over the facial plexus midway between the angle of the mouth and the zygomatic arch. This symptom is given varying grades of importance by different authors. It was present in but one instance in my cases, this being one of evident tetany.

Trousseau's Sign.—By shutting off, through pressure above the elbow or in the groin, the blood-supply to arm or leg, there ensues during the pressure or immediately on its release the typical carpal or pedal spasm, as the case may be. This also was present in but one case of my series.

Routine electrical tests were done during the months October to February, inclusive, and during June and July. It is unfortunate that they could not be carried on through the entire year in order that some conclusion might be reached as to the influence of season on the incidence of tetany and the occurrence of hyperirritability. In one series of 246 cases of tetany collected in one year 74 per cent. occurred during the months of January, February, March and April. The highest percentage (24 per cent.) occurred in March. Three of my cases of frank tetany occurred in February, two each in December and January. The incidence of hyperirritability was greatest in December.

It is not possible from the data herein contained to draw any conclusions as to the relation between the incidence of tetany according to season and that of hyperirritability of the lower grades. Information on this point would aid in interpreting the meaning of the anodal grade of irritability.

If we accept the classification of Escherich and consider as evidence of at least some degree of hyperirritability, the appearance of kathodal and anodal closure and anodal opening contractions with less than 5 milliamperes of current, my own figures would show that in January 23 per cent. of reactions showed hyperirritability; February, 24.5 per cent.; June, 9.6 per cent.; July, 17.7 per cent.; November, 16.6 per cent.; and in December, 27.6 per cent.

In October the number of tests made was too small to be of consequence. The number of tests made each month was: October, three; November, twelve; December, twenty-nine; January, seventy-four; February, fifty-seven; June, fifty-two; July, ninety.

The months of December, January and February gave the greatest number of middle-grade reactions, which corresponds in part to the months in which Escherich found the greatest incidence of tetany. Seven of my ten cases giving complete tetany reactions were under observation in these three months. Although followed up to the time of their deaths, none of these ever showed other evidences of tetany. They were all cases of malnutrition and the patients are reported to have died outside the hospital from nutritional causes. These children may represent instances of increased reaction to galvanism accompanying metabolic disturbance of severe grade and not due to the tetanoid condition. They were, however, discharged from the hospital months before death and the reports made on their condition during this time are not complete enough to positively exclude the possibility of the existence of true tetany.

Three hundred and eighteen tests were made on 118 children, being repeated more frequently on those showing a tendency to electrical hyperirritability.

The instrument used supplied galvanic current from dry cells, and contained a switch for reversing its polarity, a rheostat for controlling the current strength, and a balanced milliamperemeter measuring from 0.2 to 10 milliamperes.

Ten of our cases gave low reactions with all four tests, kathodal closure, anodal closure, anodal opening, and kathodal opening. These children were suffering from varying grades of malnutrition and all died while under observation, either in the ward or out-patient department, from nutritional causes. None of them developed other evidences of tetany.

Although Escherich describes the test as easy to perform without resistance on the part of the patient, in my subjects there was constantly so much struggling that it was difficult to find the moment of muscular relaxation necessary for the appreciation of response to the weaker currents. In a small number of cases the reactions of both left and right sides were taken and very little difference found. Escherich spoke of

considerable variation in his experience. Constant resistance necessitated mild chloroform narcosis in a few cases. The reactions obtained in this way were no lower than the average without such narcosis.

Escherich and von Pirquet considered the peroneal nerve muscle-group the best for use, and this proved the most satisfactory in my series. Erb employed the ulnar and prefers it. The median nerve has been used by Mann and Thiemich but reacts to anodal closure with less current than to kathodal closure, quite contrary to the findings in the peroneal nerve, and is in general more sensitive to electrical stimulation than the peroneal.

Muscular response was obtained at current strengths given in Table 1 in every one of the 318 tests made for kathodal closure. For anodal closure response occurred at 5 milliamperes, or lower, 149 times and failed 169 times. For anodal opening, eighty-seven results were positive and 231 negative. The reaction for kathodal opening was present only ten times and lacking in 308 instances. Table 1 shows the current strengths at which reactions were obtained.

TABLE 1.—SHOWING THE CURRENT STRENGTHS AT WHICH ELECTRICAL REACTIONS WERE OBTAINED IN CHILDREN

	Kathodal Closure	Anodal Closure	Anodal Opening	Kathodal Opening
Less than 1 milliampere	0	0	0	0
From 1 to 2 milliamperes	37	2	0	1
From 2 to 3 milliamperes	74	28	3	3
From 3 to 4 milliamperes	58	53	23	2
From 4 to 5 milliamperes	29	19	17	3
From 5 to 10 milliamperes	18	57	47	30

The peroneal nerve-muscle group was employed for the tests, the negative electrode being placed on the upper abdomen, the positive over the peroneal nerve as it passes behind the head of the fibula.

The child to be tested was laid with the feet pointing to the left of the operator, whose left hand supported the left ankle and foot of the subject in such a manner as to feel any twitch occurring in the flexors of the ankle or of the toes. Slight reactions are readily felt in this way which would be imperceptible to the eye. The positive electrode is controlled by the operator's right hand, the negative one being held in position by the assistant who with his free hand controls the rheostat. It is necessary that the tests be begun with a current of sufficient strength to produce muscular response, and gradually be reduced from this to the point at which the twitch is lost. If the reverse is attempted the lowest contraction point will be invariably passed before response occurs.

Allowance for individual skin resistance is to be made in order to avoid undue disturbance to the patient through the use of unnecessarily strong currents. This resistance varies directly with the amount of sub-

cutaneous fat, and reduces rapidly as the operation progresses, the latter fact being apparently due to the congestion which, developing under both electrodes, increases the skin's conductivity. This variation is great, both in different individuals and in the same case at the beginning and end of a test. Thus the same rheostat reading which in one instance may give a current through the body of 1 milliamperes will in another case or after the skin congestion has developed during many applications of the current allow from 6 to 8 milliamperes to pass and result in unnecessary irritation and violent resistance on the part of the subject.

The test for kathodal closure should be first made, as response to this is obtained most readily and with the least current strength. Anodal closure, anodal opening and kathodal opening should follow in order.

Infants less than a month old are less susceptible to electrical stimulation than older children, and these in turn are more susceptible than the adult.

In general there are three grades of electrical irritability:

1. The normal, in which only kathodal closure occurs under 5 milliamperes. Sometimes anodal closure is found at 5 milliamperes or just below it.

2. The middle grade or anodal hyperirritability, in which kathodal closure is less than 5 milliamperes and anodal opening is less than anodal closure and less than 5 milliamperes.

3. Tetany, in which all four reactions are less than 5 milliamperes. As suggestive of tetany is the occurrence of anodal opening less than anodal closure and the appearance of kathodal-closure tetanus.

Of the children under discussion sixty-five were boys and fifty-three girls. In 24.6 per cent. of the boys and 15 per cent. of the girls hyperirritability occurred. Of the ten patients showing the highest grade of irritability there were seven boys and three girls. There were eighteen under 1 week of age, fourteen from 1 week to one month, eleven from 1 to 2 months, thirteen from 2 to 3 months, twenty from 3 to 5 months, and fourteen each from 5 to 7, 7 to 9 and 9 to 13 months. Of the eighteen children under 1 week of age, the middle-grade reaction was obtained in no case. Of the fourteen from 1 week to 1 month it was present in 7 per cent. Of the twenty-four from 1 to 3 months old 8 per cent. showed this partial hyperirritability. From 3 to 5 months 40 per cent. of twenty cases gave the partial reaction. From 5 to 8 months 50 per cent. of the twenty-four cases evidenced anodal irritability. Of eighteen children of 8 months and older, it was obtained in 22 per cent.

The averages obtained in children of from 3 to 8 months were consistently lower than those of any other period. Those from 1 to 3 months gave the next lowest.

TABLE 2.—SHOWING ELECTRICAL REACTIONS ACCORDING TO AGE

	Average	Number of Tests
Under one week, 18 children—		
Kathodal Closure	3.6	25
Anodal Closure	4	5
Anodal Opening	4.9	4
Kathodal Opening	5 +	all
One week to one month, 14 children—		
Kathodal Closure	4.5	14
Anodal Closure	6.9	10
Anodal Opening	6.3	3
Kathodal Opening	7	1
One month to 3 months, 24 children—		
Kathodal Closure	3	44
Anodal Closure	4.3	26
Anodal Opening	5.3	17
Kathodal Opening	4.5	2
Three months to 5 months, 20 children—		
Kathodal Closure	2.7	42
Anodal Closure	3.9	34
Anodal Opening	4.4	17
Kathodal Opening	1.3	1
Five months to 8 months, 24 children—		
Kathodal Closure	2.9	70
Anodal Closure	3.5	56
Anodal Opening	4	33
Kathodal Opening	3.4	4
Eight months and over, 18 children—		
Kathodal Closure	3.8	24
Anodal Closure	4.5	18
Anodal Opening	4.6	9
Kathodal Opening	5	1

Escherich's conclusions as to the reactions of normal children are:

1. The first weeks do not differ from the later weeks of life in electrical irritability.
2. In normally developing children only kathodal closure is less than 5 milliamperes.
3. Anodal closure at less than 5 milliamperes is seldom found in the peroneal nerve during the first year.
4. Opening contractions are seldom found at less than 5 milliamperes.

My experience seems to indicate that children less than 1 week old are less sensitive to electrical stimulation than when older. Anodal closure was elicited 100 times at a point less than 5 milliamperes. Anodal opening was found fifty-three times, and kathodal opening ten times. This variance of these results with those of Escherich may be due to the fact that my children were, as before stated, far from normal, in that they were all in the ward because of nutritional disturbances. To this point reference will be made later.

There were in this series six infants weighing less than 5 pounds, seventy-one between 5 and 10 pounds, and twenty-three of 10 pounds and over.

The incidence of partial hyperirritability in children under 5 pounds was 16 per cent.; 5 to 10 pounds, 22 per cent.; 10 pounds and over, 30 per cent.

With reference to change in weight or, as this is its best index, the general condition of the subjects, it was found that of the sixty children losing weight, 25 per cent. showed partial hyperirritability; of the twelve with stationary weight, 16 per cent. showed partial hyperirritability; and of the twenty-seven gaining weight, 37 per cent. showed partial hyperirritability.

During the period of this work there were fifty-seven infants on skim-milk mixtures, twenty-one on condensed milk, twenty-three on butter-milk, eighteen on Finkelstein's "Eiweismilch," fourteen on whole milk mixtures and twenty-four were on the breast. As it has been shown that tetany occurred more frequently in artificially than in breast-fed children, comparisons between the reactions of these classes were made. In the breast-fed the average of kathodal closure, 3.2 in thirty-eight tests; anodal closure, 4 in twenty-four tests; anodal opening, 4 in seven tests; and kathodal opening, 2.4 in one test, were practically the same as those for artificial feeding, which were: kathodal closure, 2.8 in 172 tests; anodal closure, 3 in 123 tests; anodal opening, 4 in sixty tests; and kathodal opening, 4 in nine tests. These averages of the values found to obtain in the individual tests are given to show something of their individual variation. Taking the number of breast and artificially fed children who showed distinct hyperirritability, it appears that there was none of the ten former, but 24 per cent. of the 108 of the latter class. It must be added, however, that the cases were not exclusively on either type of nourishment for a great length of time before testing.

Referring again to the nutritive condition, the reactions were classified as to good and poor gastric and intestinal digestion. There were thirty-eight in which the gastric digestion was good, fifty-eight in which it was poor. Twenty-seven children had satisfactory intestinal conditions and in seventy-seven the opposite was the case.

Again leaving the questionable average figures and dividing these classes of digestive condition into those showing hyperirritability and those reacting to kathodal closure alone, it appears that of thirty-eight instances of good gastric digestion 30 per cent. showed hyperirritability; of fifty-eight instances of poor gastric digestion 30 per cent. showed hyperirritability; of twenty-seven instances of good intestinal digestion 33 per cent. showed hyperirritability; of seventy-seven instances of poor intestinal digestion 24 per cent. showed hyperirritability.

Reviewing the tabulations concerning size, gain or loss in weight, digestive condition and method of nourishment, it is apparent that they throw little if any light on the relation of these conditions to electrical irritability. The strong impression was gained, however, during the

progress of the work, that the child's irritability varies directly with the general condition of nutrition, and that the perfectly developed, well-nourished subject gives response much less readily to galvanism than if under-fed and of low body weight.

It is evident that from this compilation nothing can be stated in respect to nutrition and electrical irritability, except that a considerable series of tests showed no influence of the one on the other.

TABLE 3.—SHOWING THE ELECTRICAL REACTIONS UNDER VARYING CONDITIONS OF DIGESTION AND NUTRITION

	Average	Number of Tests
With good gastric digestion—		
Kathodal Closure	2.8	88
Anodal Closure	5.3	60
Anodal Opening	3	39
Kathodal Opening	3.6	4
With poor gastric digestion—		
Kathodal Closure	3	133
Anodal Closure	3.6	111
Anodal Opening	4.3	53
Kathodal Opening	3.6	5
With good intestinal digestion—		
Kathodal Closure	3	38
Anodal Closure	4.1	44
Anodal Opening	4.1	28
Kathodal Opening	4.2	1
With poor intestinal digestion—		
Kathodal Closure	2.2	140
Anodal Closure	3.6	111
Anodal Opening	4.6	50
Kathodal Opening	3.6	4

TABLE 4.—SHOWING AVERAGE OF REACTIONS IN TABLE 3, GROUPING GASTRIC AND INTESTINAL TOGETHER

	Average	Number of Tests
With good gastric and intestinal digestion—		
Kathodal Closure	4.9	126
Anodal Closure	3.7	104
Anodal Opening	3.3	67
Kathodal Opening	3.9	5
With poor gastric and intestinal indigestion—		
Kathodal Closure	2.6	273
Anodal Closure	3.6	222
Anodal Opening	4.4	103
Kathodal Opening	3.6	9

SUMMARY

1. Tetany is seen in about 2 per cent. of infants under 1 year.
2. An early and definite diagnosis depends on the presence of marked electrical hyperirritability.
3. Normal children react to kathodal closure alone at less than 5 milliamperes.
4. Many children not having tetany give low response to anodal closure and in fewer cases to anodal opening.

5. This partial or anodal grade of irritability may depend on factors entirely foreign to tetany for its causation, or may mark the early stages of the disease.

6. Infants of less than 1 month respond less readily to galvanism than do older children.

7. Kathodal opening contraction may be absent in true tetanoid conditions.

8. The degree of hyperirritability may vary greatly in the same case from time to time.

9. No constant difference was found in the reactions obtained on left or right sides.

10. Anesthesia does not affect electrical irritability.

11. The peroneal group is best adapted for the test.

12. Three points in the technic are important:

(a) The test must start with a current strength able to produce muscular response and must be carried on with reducing current strength to the point at which muscular response fails.

(b) As the skin conductivity is constantly increasing care must be taken to avoid undue and strong stimulation as the test progresses.

(c) Kathodal closure, anodal closure, anodal opening and kathodal opening should be tried in the order of ease of eliciting and the amount of current strength required; that is, in the order named.

13. The highest incidence of tetany is during the early months of the year.

THE ELECTRICAL REACTIONS IN PARATHYREOPRIVA DOGS

A series of experiments on normal dogs, and on those deprived of part or all of their parathyroid tissue, was made with the object of determining:

1. The electrical irritability of the normal dog.

2. The influence on this irritability of the removal of one or more of the parathyroid glands.

3. The interval elapsing before the electrical evidences of tetany appeared.

4. The amount of time by which these symptoms antedated the physical evidences of the disease.

5. Whether the remaining glands would show evidences of attempt at compensatory hypertrophy.

The galvanic reactions of these dogs, taken for several days before operation to establish the normal for each animal before testing for abnormal reactions, followed very closely the normal reactions of the children tested in the ward. The same nerve muscle-group as that in the case of the child was used, the peroneal, the negative electrode being placed on the abdomen. No difficulty was met in getting accurate readings so long as the skin at the site of contact of the electrodes was kept closely shaven. It was unnecessary to use an anesthetic for the tests, and in the few cases in which mild anesthesia was used, for reasons of comparison, no change in the response to the current was observed.

Following the method used by McCallum, and in the belief that in the short time that these animals lived after operation no influence due to hypothyroidism would cloud the findings, thyroid and parathyroid glands were removed together. On account of the length of time necessary for such observations, it was not possible to include in this paper the *ultimate* results on the electrical reactions of simple partial parathyroidectomy. This will be made the subject of a later report.

The average reaction to kathodal closure before operation was from 1 to 3 milliamperes; for anodal closure, 3 to 4 milliamperes; for anodal opening, 4 to over 5 milliamperes; for kathodal opening, always over 5 milliamperes.

In one of the animals tested, only one parathyroid was removed, and in five cases, two parathyroids, with one lobe of the thyroid, were taken out. The intention here was to determine the effect on the electrical irritability of the nervous system of a lesion in a part of the parathyroid tissue. The animal with a single parathyroid gland removed showed only partial electrical irritability for 236 hours after operation, but there was immediate hyperirritability after the removal of the remaining three glands.

Of the semi-parathyreopriva dogs all five showed an electrical hyperirritability toward anodal closure and anodal opening. The kathodal reactions showed change in only two instances (Dogs 6 and 7). In two cases kathodal tetanus was elicited after the first operation, although it had not been obtained before the parathyroids were partially removed. This hyperexcitability to anodal stimulation appeared in from one to three days after removal of the two glands, and corresponds to Escherich's mild "*Anodische grad.*"

In no case was there any evidence of tetany other than the changed electrical irritability. Lesions of one or two parathyroid glands may, then, produce moderate increase of electrical excitability to the galvanic current, but do not at once result in general tetany. In two instances (Dogs 6 and 7) partial thyreo-parathyroidectomy was followed by the complete tetany reaction. These animals might have furnished examples of tetany due to partial removal of the parathyroid tissue had the second operations been longer deferred. In every case of partial removal of the glands there appeared, in varying degree, some tendency to anodal irritability. Two of McCallum's semi-parathyroidectomized dogs showed tetany in two days after operation on the glands of one side.

In four dogs both lobes of the thyroid, with entire capsule and all four parathyroid glands, were removed at one operation. Electrical hyperirritability to all four types of current supervened in from five to forty-eight hours after operation, with one exception. The electrical tests showed tetany from a few hours to two days before any other symp-

toms of the condition appeared. One of these four dogs showed slight laryngospasm on the sixth day following operation, but up to the fourteenth day gave no typical increased response to electrical stimulation. He was then given 2.5 gr. of thyroid extract daily to counteract any effect of the loss of the thyroid secretion, and did for four days respond to currents of lesser strength. This, however, did not persist, and the animal died on the forty-sixth day after operation without having shown any ill effect from the removal of all his parathyroid tissue. A careful autopsy failed to show any accessory glands in the neck, the thymus or elsewhere, or to furnish any additional clue as to the cause of the sudden death of the animal.

After the removal of all four glands, nine animals gave low electrical reactions, from which a diagnosis of tetany could be made in twenty-seven, twenty-one, twenty-two, sixteen, twenty-nine, nineteen, seventeen, nineteen, nineteen, hours after removal. In one instance (Dog 3) kathodal closure, anodal closure, anodal opening, dropped to 0.4 milliamperes in twenty-six hours after operation and the animal died in tetany, but kathodal opening remained over 5 milliamperes.

Partial thyreo-parathyroidectomy was done on six dogs and the operation made complete, respectively, in four, five, twelve, twelve, thirteen and thirteen days later.

Measurements of the lobes of the thyroid and of the parathyroid glands first removed were compared with those left till the second operation. Search was also made in sections from all glands for mitosis and evidences of glandular over-activity. In each case there was evident hypertrophy of the remaining lobe of the thyroid, but there were found no evidences of attempt at similar change in the remaining parathyroid glands.

The accompanying charts indicate that the electrical reaction of animals subjected to parathyroid injury of varying degree do not change *pari passu* with the lesion produced, although Biedl and others have found that the general picture of tetany depends for its intensity on the number of glands removed. It was found, in the majority of cases, that after partial operation the reactions were only in small degree changed till the remaining glands were removed, when sudden tetany developed.

As it has been observed by several experimenters that parathyroidectomized animals often do not show symptoms of tetany till subjected to some metabolic or physical strain, electrical tests on the partially parathyroidectomized dogs were made after considerable muscular exertion. The nervous excitability was not found increased by such exercise, although tachypnea, muscular spasm, and laryngospasm were frequently induced or augmented. The response to galvanism is, then, less influenced by intercurrent conditions than other tetany symptoms.

Electrical hyperirritability resulting on removal of all parathyroids appeared in nine of the ten dogs tested, sixteen, six, twenty-four, and twenty hours and one, one, two, three, and four and one-half days, respectively, before the development of other tetanoid signs.

The average time of onset, after complete operation, of electrical hyperirritability, was thirty-three hours. The average for the same in cases in which the operation was done in two stages was twenty hours. Inasmuch as in the short time allowed to elapse between operations in this series of experiments there seems to have been produced a disposition

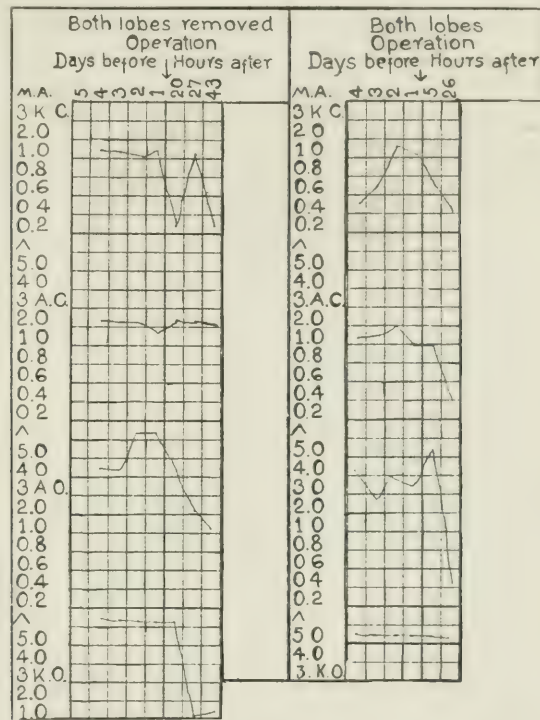


Chart 1, Dog 1.—Electrical reactions after complete extirpation of glands. weight of dog 22 pounds; killed forty-eight hours after operation; no signs of frank tetany. Electrical hyperirritability preceded death sixteen hours.

Chart 2, Dog 2.—Weight 27.5 pounds; died in tetany thirty-one hours after operation. Electrical irritability preceded tetany six hours.

to immediate response to further injury, it is possible that more time would have allowed the development of tetany reactions after only partial extirpation of the parathyroids.

Symptoms referable to the hyperirritability of nerve centers were, then, in every instance, the first to appear, and although in this series of tests they preceded other symptoms by an apparently short time, it is

to be remembered that in no case was the course of the disease produced longer than sixteen days, the average being nine days. The average of the times occupied in the development of electrical hyperirritability was one-ninth of the times lapsing before the production of other symptoms.

The galvanic current is, then, of especial value in the early diagnosis of tetany.

ANALYSIS OF PARATHYREOPRIVA DOGS

A. COMPLETE EXTIRPATION OF GLANDS

DOG 1.—Female, weight 22 pounds. August 11, reactions were obtained at kathodal closure, 1; anodal closure, 2; anodal opening, 3; kathodal opening, over

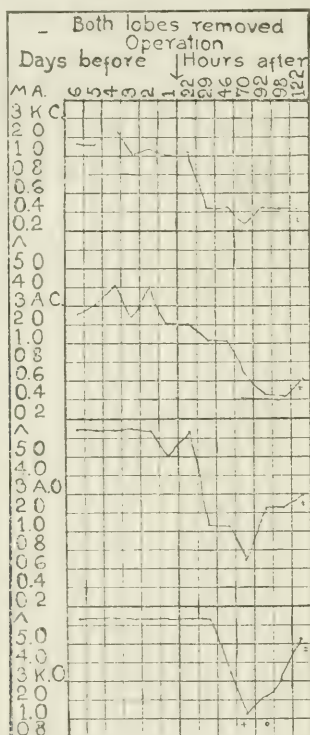


Chart 3, Dog 3.—In the above chart "o" = no general tetany; + = general tetany; ‡ = tests made as dog was dying, showing further reduced reaction to opening contractions.

5 milliamperes. Under ether anesthesia anodal tetanus was obtained at anodal opening, 3 milliamperes; the other reactions being unchanged.

August 12, closing contractions somewhat lower, opening contractions over 5 milliamperes. No change with ether anesthesia.

August 15 and 16, reactions the same. The average for this animal's galvanic response was kathodal closure, 1; anodal closure, 2; anodal opening, 4; kathodal opening over 5 milliamperes.

August 16, both lobes of thyroid with capsule were removed and found to include four parathyroid glands all lying on surface of thyroid.

August 17, twenty hours after operation, there was no evident tetany. The reactions were, kathodal closure, 2; anodal closure, 2; anodal opening, 4; kathodal opening over 5 milliamperes. Twenty-seven hours after operation there was further evidence of electrical hyperirritability, reactions being obtained at kathodal closure, 1; anodal closure, 2; anodal opening, 1; kathodal opening, 1.1.

August 18, forty-three hours after operation, there was fine tremor, slight rigidity and tachypnea, with reactions practically the same as those of the preceding day. On account of considerable distress the dog was killed two days after operation.

Dog 1 showed electrical hyperirritability 20 hours after operation and one day before there was other evidence of tetany.

Dog 2.—Male, weight 27 pounds. The average of the reactions taken on each of the four days before operation was, kathodal closure, 1; anodal closure, 2.4; anodal opening, 3.6; kathodal opening over 5 milliamperes.

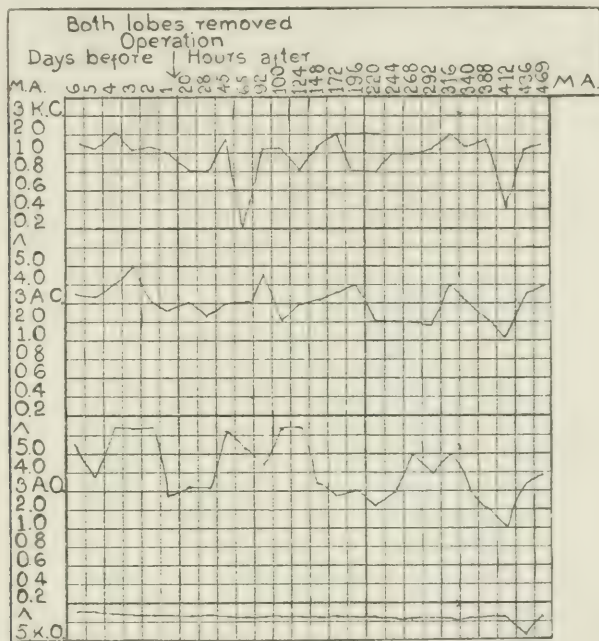


Chart 4, Dog 4.—In the above chart the cross (x) indicates that 2.5 gr. thyroid extract was given daily; dog weighed 6 pounds; died forty-six days after operation suddenly, having had no signs of tetany other than laryngospasm.

August 18, complete thyreo-parathyroidectomy was done, four glands being identified. Five hours after operation the reactions were, kathodal closure, 3; anodal closure, 2; anodal opening, 5; kathodal opening over 5 milliamperes. Twenty-three hours after operation the reactions were, kathodal closure, 2; anodal closure, 2; anodal opening, 2; kathodal opening, over 5 milliamperes. Twenty-seven hours after operation muscular twitchings were noticed and the animal died in convulsions and general tetany four hours later.

This dog showed an unusually prompt onset of electrical hyperirritability and frank tetany with death in severe muscular spasm in thirty-one hours after operation. With the exception of kathodal opening, the reactions were very low, but the former never dropped below 5 milliamperes, although the physical evidences of tetany were severe.

Dog 3.—Six observations during the week preceding operation showed the normal reactions to be, kathodal closure, 1.3; anodal closure, 2.4; anodal opening and kathodal opening over 5 milliamperes.

August 23, both lobes of thyroid with four parathyroid glands were removed.

August 24, twenty-two hours later, there was increased excitability to closing, but none to opening tests. Twenty-nine hours after operation, however, all tests responded to currents of less than 1 milliampere, excepting kathodal opening, which remained above 5 milliamperes.

August 25, forty-six hours after operation, kathodal opening dropped to 3 milliamperes, and seventy hours after operation, all reactions were below 1

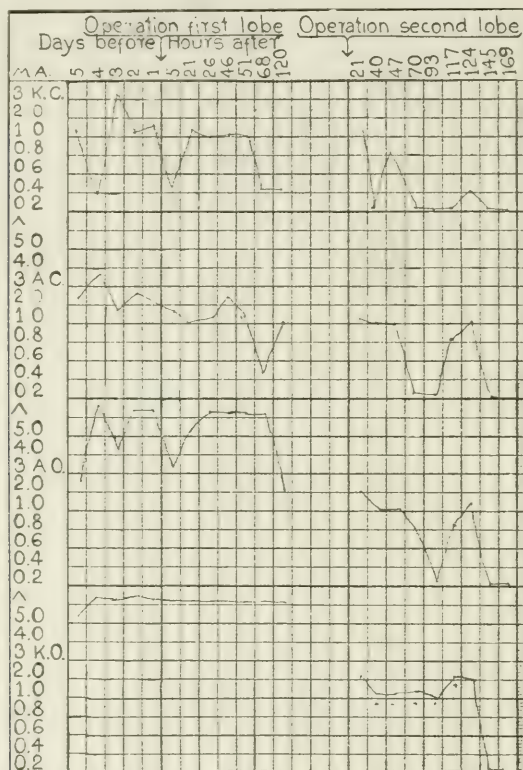


Chart 5, Dog 5.—Weight 32 pounds. x = occurrence of tetany (kathodal); first evidence of frank tetany four days after second operation; dog killed 169 hours *post operatione*.

milliampere. From this time on to the death of the dog the reactions remained about the same. Tests made at a few moments previous to death gave still further reduced reaction to opening contractions.

Frank tetany appeared forty hours after operation and persisted throughout. In this case the electrical indications of tetany preceded only by a few hours the physical symptoms of the disease.

This dog evidenced early and marked response to parathyroid lesion by electrical hyperirritability and only five hours later all tetany symptoms were pronounced.

Dog 4.—Female, weight 6 pounds. Daily observations for six days preceding operation gave this animal a normal average of kathodal closure, 1.2; anodal closure, 3; anodal opening, 5; kathodal opening over 5 milliamperes.

August 24, complete thyreo-parathyroidectomy was performed and for six days no change was noticed other than slight increased responsiveness to kathodal closure and anodal closure. On the sixth day moderate laryngospasm developed and this persisted as the only symptom of tetany till death, which occurred on the forty-sixth day after operation. Autopsy failed to show the existence of accessory parathyroids. Fifteen days after operation $2\frac{1}{2}$ gr. of thyroid extract was given daily to counteract any effect of the loss of the thyroid lobes. This had no effect on the general condition.

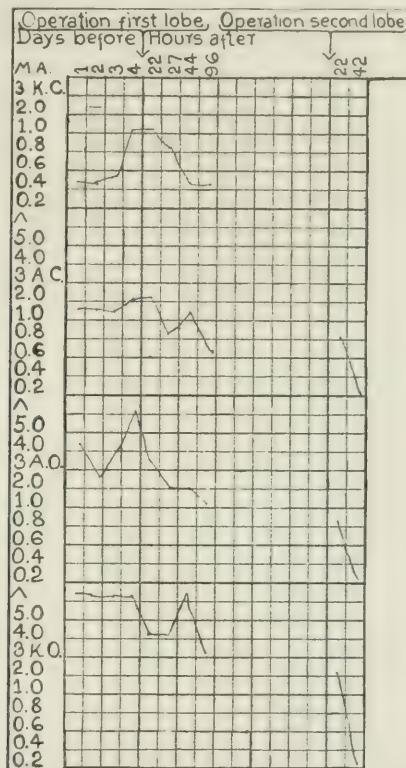


Chart 6, Dog 6.—Weight 30 pounds. Killed in tetany forty-eight hours after second operation. Electrical hyperirritability preceded tetany forty-four hours.

This animal alone failed to develop electrical hyperirritability or marked tetany symptoms after suffering loss of all the parathyroid glands.

B. DOGS IN WHICH PARATHYROIDECTOMY WAS DONE IN TWO STAGES

Dog 5.—Male, weight 32 pounds. For the six days preceding operation the average reactions were found to be, kathodal closure, 1; anodal closure, 3; anodal opening and kathodal opening over 5 milliamperes; i. e., relatively low closing contractures.

August 17, the right lobe of the thyroid with capsule was removed, two parathyroid glands being identified. Through the slipping of a ligature there was severe hemorrhage, without, however, any ill effects being manifest, then or

later. There was a gradual rise in electrical excitability for kathodal closure, anodal closure, and anodal opening for five days. At the end of this time the figures being, respectively, 0.4, 1, and 2 milliamperes. There were no other signs of the tetany condition. On August 22, the remaining lobe of thyroid, which was markedly hypertrophied and contained one parathyroid, was removed. Again, such severe hemorrhage occurred as to make recovery doubtful.

Twenty-one hours after the second operation the electrical diagnosis of tetany was definite, with kathodal closure, 1.4; anodal closure, 1.1; anodal opening, 2.1; kathodal opening, 2.1 milliamperes. The reaction points dropped steadily until August 29, when all were obtained at .2 milliamperes.

No physical evidences of tetany were noted till August 26, when there was some tachypnea. On August 29, the dog was stupid, emaciated and would not eat, but had no definite tetany symptoms. He was chloroformed at this time.

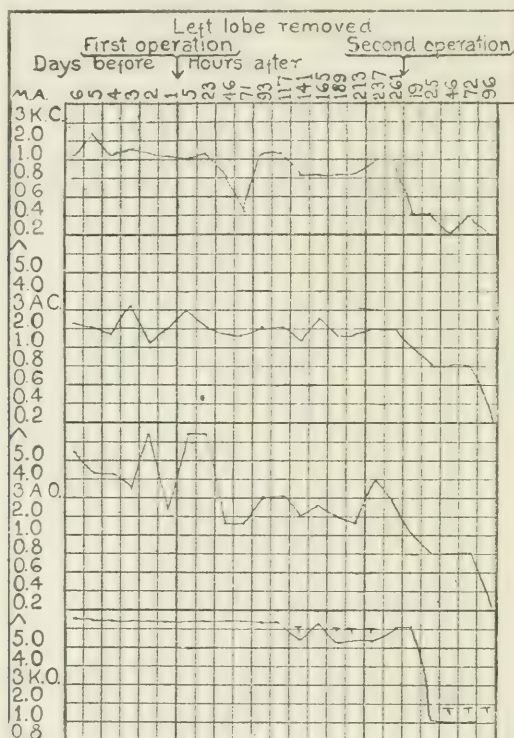


Chart 7, Dog 7.—Died in tetany ninety-six hours after second operation. "T" = kathodal tetanus.

For four days preceding the second operation this dog was evincing an increasing electrical hyperirritability which continued uninterruptedly after the second operation. Although the electrical reactions had been strong for tetany, for nine days there was no other evidence of the condition, until August 26, when mild tachypnea developed. McCallum has shown that the muscular spasm, convulsions, etc., of experimental tetany can be controlled and temporarily relieved by bleeding. The second severe hemorrhage may in this case explain the absence of frank tetany. If this supposition be granted, it is of interest and consequence to note that the loss of blood exerted no influence on the course or the development of the nervous hyperexcitability.

Dog 6.—Female, weight 30 pounds. The mean reaction before operation was found to be kathodal closure, 1.4; anodal closure, 2; anodal opening, 4; kathodal opening over 5 milliamperes. On August 18, the thyroid and parathyroids of the left side were removed. During the following four days there was distinct increase of the electrical hyperirritability, the reactions being, kathodal closure, .4; anodal closure, .6; anodal opening, 1; kathodal opening, 5 milliamperes. This increased irritability began twenty-seven hours after operation. August 22, the remaining lobe of the thyroid, with its parathyroids, was removed and, at once, all reactions dropped to .2 milliamperes. No other signs of tetany were present till two days after the second operation.

This dog responded markedly in her nervous excitability to the removal of part of her parathyroid tissue, and gave low reactions for four days before muscu-

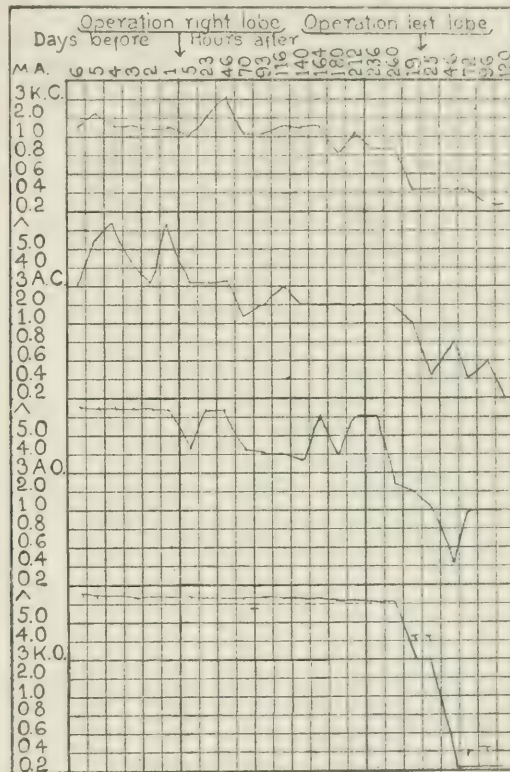


Chart 8, Dog 8.—Weight 16 pounds; found dead September 12, 120 hours after second operation, never having shown signs of apparent tetany.

lar spasm appeared. Moderate hypertrophy of the remaining thyroid lobe was noted, but no change was apparent in the parathyroids.

Dog 7.—Male, weight 11 pounds. Six tests gave for this animal kathodal closure, 2; anodal closure, 2; anodal opening, 5; kathodal opening over 5 milliamperes as the average normal.

August 24, the left lobe of the thyroid and only one parathyroid were removed. During the ten days following operation there was constantly increasing irritability, most marked in the low anodal opening contraction and kathodal opening tetanus. No other tetany symptoms were noticed. September 6 the right lobe

kathodal closure, .8; anodal closure, 1; anodal opening, 1; kathodal opening, 2 milliamperes. Forty hours after operation there was partial paralysis of the front legs, with electrical reaction, all below .2 milliamperes.

Here, again, injury to a portion of the parathyroid glands caused none of the phenomena of tetany, but apparently prepared the way for a very rapid and severe reaction on the ablation of the remaining glands.

Dog 10.—Female, weight 18 pounds. This dog's reactions before operation were; kathodal closure, 1; anodal closure, 3; anodal opening, 5; kathodal opening, over 5 milliamperes. After removal of the left half of the thyroid and parathyroid tissue, the reactions of kathodal closure, anodal closure, and anodal opening were somewhat irregular, with kathodal opening unaffected, until the extirpation of the remaining glands, nine days later. Nineteen hours after second operation there was marked hyperirritability, and a day and a half later

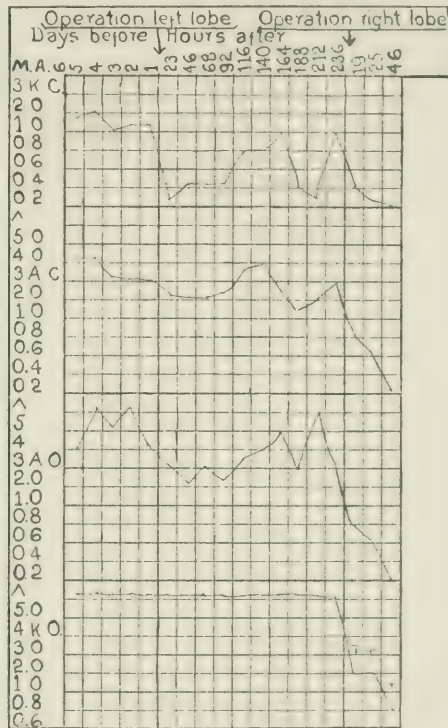


Chart 10, Dog 10.—Weight 18 pounds; frank tetany came on seventy hours (killed) after second operation.

electrical reactions were obtained below .8 milliamperes, and there was severe general tetany.

SUMMARY

1. The reactions in normal dogs are similar to those of normal children.
2. The peroneal nerve muscle-group is best suited to the test.
3. Mild anesthesia does not increase the delicacy of the test.
4. Both sides of the body react alike.

5. In normal dogs kathodal closure averages at from 1 to 3 milli-amperes; anodal closure from 3 to 4; anodal opening from 5 to over 5, and kathodal opening is always over 5 milliamperes.

6. The complete extirpation of the parathyroid glands produces prompt hyperirritability.

7. Partial extirpation of the parathyroid glands produces either anodal irritability or only inconstant change.

8. Complete extirpation, following partial removal of the glands, results in more immediate hyperirritability than when all glands are removed at once.

9. Increased irritability follows the complete parathyroid extirpation in an average of thirty-three hours.

10. Electrical hyperirritability follows the second of the two-stage operation in an average of twenty hours.

11. Electrical change always precedes the other symptoms of tetany by considerable time.

159 East Seventh Street.

TWO CASES OF INFLUENZAL MENINGITIS — PATIENTS TREATED WITH HEXAMETHYLENAMIN

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In a former communication¹ one of us reported a case of meningococcus meningitis treated with hexamethylenamin. This treatment was suggested by the work of Crowe,² who showed that the drug appeared in considerable quantity in the cerebrospinal fluid shortly after administration. In the case reported there appeared to be some benefit derived from the treatment, and hexamethylenamin could be readily demonstrated by Hehner's test in the fluid from lumbar puncture, even when diluted forty times. The patient lived twenty-six days, although the attack was very acute. This experience led us to use hexamethylenamin in the treatment of two subsequent cases of influenzal meningitis. The quantities used were relatively much larger than in the case of meningococcus meningitis, for we were influenced by the work of Frothingham,³ who showed by experiments on animals that larger quantities could probably be used with safety.

REPORT OF CASES

CASE 1 (Chart 1).—H. B., No. 22,123, negro child, 18 months old, born in Jamaica, in Panama 12 months, admitted to Colon Hospital Feb. 3, 1910.

History.—Patient had been a healthy child previously; for about two weeks had had a "cold" and some fever; had one convulsion on the day of admission.

Examination.—Well nourished negro child, large head with prominent forehead and prominent parietal bosses; no other signs of rickets; the fontanelles were closed. The pupils seemed equal and there was no strabismus. A few scattered râles were heard in the lungs. The heart, abdomen, liver and spleen seemed normal. The left leg and arm appeared to be paralyzed. There was no opisthotonos, no stiffness of the neck, the patellar reflex was normal, no ankle clonus, Kernig's sign was absent, and Babinski's sign variable. Stained blood films were negative for malarial parasites. The urine contained a trace of albumin.

Summary of Course of Illness.—Chart 1 shows the temperature curve, the pulse and respiratory rates, and the administration of hexamethylenamin, which did not appear to affect the course of the disease. Convulsions were numerous during the illness; they ceased for three days after the first lumbar puncture and then recurred. During the convulsions the apparently paralyzed left leg and arm were moved most violently. Towards the end the patient was in a state of tonic muscular rigidity, the feet were drawn downward and could not be flexed.

*Read at a meeting of the Medical Society of the Isthmian Canal Zone, April, 1911.

1. Brem: New York Med. Jour., 1910, xcii, 816.

2. Crowe: Bull. Johns Hopkins Hosp., 1908, xix, 109.

3. Frothingham: Arch. Int. Med., 1909, iv, 510.

made out. The patient became markedly emaciated and died on the ninth day after admission.

Diagnosis.—The diagnosis at first lay between acute anterior poliomyelitis and cerebrospinal meningitis, and the differentiation was made only by lumbar puncture.

Leukocyte counts: February 5, 20,000; February 6, 10 a. m., 24,000; February 6, 5 p. m., 19,800; February 7, 10 a. m., 20,600.

Lumbar punctures: February 5, 5 p. m., 30 c.c. of moderately turbid whitish fluid under increased pressure; cells 3,700 per c.mm., nearly all polymorphonuclear leukocytes with bizarre and fragmented nuclei. Smears from centrifugalized specimen negative for tubercle bacilli. In a smear stained by Gram's method and counterstained with Bismarck brown, a number of cells were found which contained one each of what appeared to be Gram-negative diplococci like meningococci. No extracellular organisms were found and it could not be determined whether the meningococcus-like bodies were organisms or fragments of nuclei. The fluid soon showed a filmy white coagulum with which blood-serum was inoculated. No growth appeared.

February 6, 10 a. m., lumbar puncture again showed turbid white fluid under high pressure; about 50 c.c. was obtained. Cells numbered 3,500 per c.mm. A filmy white coagulum formed quickly and was used to inoculate blood-serum and for smears. Again no growth appeared on the blood-serum. The smears showed numerous polymorphonuclear leukocytes with bizarre and fragmented nuclei. One body that looked extremely like an intracellular meningococcus was found. A smear stained for tubercle bacilli was negative. At the time of the puncture, 30 c.c. of Flexner's antimeningitis serum was introduced easily without anesthesia.

February 7. A further and more exhaustive search of smears made from the spinal fluid obtained February 5 was negative at first for definite organisms. Again, a number of cells were seen which contained what appeared to be single pairs of Gram-negative diplococci, but the possibility that they were fragmented portions of nuclei could not be excluded. One cell with two pairs of the bodies was found. Finally a small group of extracellular Gram-negative bodies like very small bacilli was noticed, and on further examination it was found that these were bacilli and that others were fairly numerous in smears from the fluids of the punctures of both February 5 and February 6. They were very small and were but faintly stained by the Bismarck brown counterstain and by the methylene blue stains. They had been overlooked in the search for the common and more apparent organisms of meningitis, meningococci, pneumococci, and pyogenic cocci. Cultures on blood-agar were made immediately from the fluid of February 5, and minute, discrete, "dew-drop" colonies typical of *B. influenza* appeared.

3 p. m. Lumbar puncture yielded 12 or 15 c.c. turbid white fluid not under increased pressure; 3,980 cells per c.mm., nearly all polymorphonuclears with bizarre nuclei. Smears showed fairly numerous extracellular and a few intracellular Gram-negative small bacilli. They were frequently attached to the periphery of the leukocytes. Cultures were made on agar-agar and blood-agar. No growth appeared on the agar-agar, but on blood-agar the typical colonies of *B. influenza* developed in pure culture. Treatment with hexamethylenamin was begun (see Chart 1), 5 gr. by intramuscular injection and 5 gr. per rectum every four hours.

February 8, 7.30 p. m. An attempt to obtain fluid by lumbar puncture failed, only a few drops escaping from the needle.

February 9. Five c.c. turbid fluid, same character as before. Hehner's test for hexamethylenamin positive.

February 11. Needle inserted several times, but only a few drops of spinal fluid could be obtained. A few drops of fluid escaped from the hole left by the needle when it was withdrawn. This fluid appeared to be purulent.

Autopsy.—The autopsy was made fourteen hours after death. The entire surface of the brain and cord was covered uniformly by an extraordinary massive, greenish, fibrino-purulent exudate that stripped off in a solid layer. The surface

of the brain beneath was injected and pinkish in color with visible engorged capillaries. The lateral ventricles were distended by a large quantity of turbid fluid. The brain tissue was soft, almost gelatinous. There were some epicardial hemorrhages, a fibrino-purulent exudate in the right pleura, and areas of bronchopneumonia in both lungs, amounting almost to a lobar pneumonia of both lower lobes. The spleen was not enlarged; the liver seemed normal; the kidneys were normal in size, pale, capsule stripped easily, cortex and pyramids normal. There was acute peribronchial lymphadenitis. Cultures from the meninges showed minute "dew-drop" colonies on blood-agar. *B. influenza* was in pure culture.

Bacteriologic Studies.—Cultures on blood-agar from the spinal fluid obtained February 5 and 7 and from the meninges at autopsy showed pure growths of minute, discrete, "dew-drop" colonies of a small, non-motile, Gram-negative bacillus. No growth appeared on agar-agar, blood-serum or in bouillon. A slight growth developed in bouillon to which blood had been added. The bacilli frequently grew in long threads, and many showed typical "safety-pin" forms. It was found that they stained well when undiluted carbol fuchsia was steamed a few seconds on the smear, and the stain washed rapidly with very dilute acetic acid. The cultures died out quickly when not transplanted at short intervals every two or three days. A guinea-pig remained well after being inoculated intraperitoneally with about 1,000 million bacilli suspended in normal salt solution. These bacilli had grown for twenty-four hours on human blood-agar. The growths were never vigorous.

CASE 2 (Chart 2).—F. T., No. 26,970, negro child, 23 months old, male, born in Colon, admitted to Colon Hospital Aug. 27, 1910.

History.—The patient had been ill for six days. The onset was with a "cold," but no cough. There was some fever and a chill two days after onset.

Examination.—On admission there were no definite meningeal signs. The patient was a well nourished, healthy looking child. He moved his limbs well. The heart and lungs were normal; the spleen was palpable (?); the blood was negative for malarial parasites, and the stool was negative for ova and parasites.

September 1. Until this time nothing definite pointing to a diagnosis had developed. Quinin and euquinin had been given without effect. The possibility of typhoid was considered. On September 1 there was some stiffness of the neck, the leukocytes were 17,000 per c.mm., and a differential count showed polynuclear neutrophils 84.6 per cent., small mononuclears 10.3 per cent., large mononuclears 5 per cent. Although there were no abnormalities of the eyes and Kernig's and Babinski's signs were negative, a lumbar puncture was made and about 5 c.c. of turbid white fluid was obtained. The cells were nearly all polymorphonuclear cells with bizarre nuclei. No diplococci were found, but there were a few small Gram-negative bacilli like influenza bacilli. The cultures on blood-serum and blood-agar showed no growth. Hexamethylenamin was ordered to be given intramuscularly in 5 gr. doses every four hours.

September 2. The head was retracted and there was some arching of the back, no strabismus, heart and lungs negative, Kernig's and Babinski's signs not present, no clonus, patellar reflex increased. Lumbar puncture; about 3 c.c. of turbid fluid obtained; cells nearly all polymorphonuclears; small Gram-negative bacilli were more numerous than on the day before; they were both intracellular and extracellular. Cultures on blood-agar showed "dew-drop" colonies in twenty-four hours; negative on blood-serum. The phenylhydrazin hydrochlorid test⁴ for hexamethylenamin was positive when one part of fluid was diluted with four parts of water. Positive tests with the spinal fluid developed slowly, but could be hastened by acidifying and heating beforehand. This indicated that hexamethylenamin was present as such and not as formaldehyd in the spinal fluid.

September 3. Marked retraction of the head and arching of the back; pupils equal, no strabismus; no ankle clonus, no Babinski's sign; there was a suggestion of Kernig's sign; heart and lungs negative; spleen not palpable. Lumbar puncture: About 20 c.c. of turbid fluid was obtained; the cells were numerous and

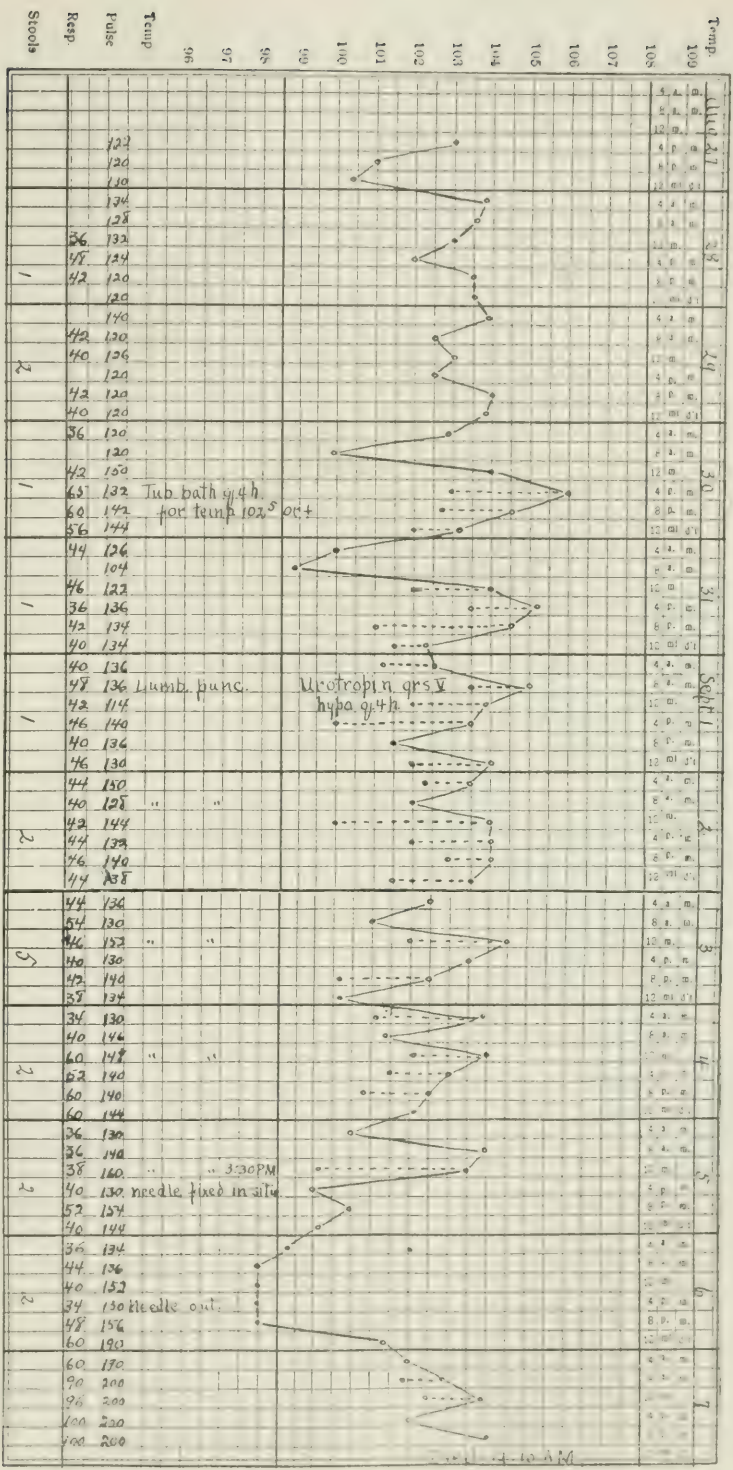


Chart 2.—Showing temperature curve, respiration and pulse-rate in Case 2, a negro child (No. 26,970), admitted to Cohen Hospital Aug. 27, 1910.

nearly all polymorphonuclears; there were numerous small Gram-negative intracellular and extracellular bacilli. The phenylhydrazin hydrochlorid test⁴ for hexamethylenamin was positive in a 1 to 20 dilution of the fluid. Cultures on blood-agar showed "dew-drop" colonies of small Gram-negative bacilli in twenty-four hours.

September 4. Râles were present throughout the lungs; there seemed to be impaired resonance at the angle of the left scapula where the breath sounds were harsh. There was marked retraction of the head, which was drawn to the left side; arching of the back; Kernig's sign present; no Babinski's sign; no ankle clonus; pupils equal; no strabismus. Lumbar puncture: 3 c.c. turbid fluid obtained; numerous small Gram-negative bacilli present; test for hexamethylenamin positive in 1 to 20 dilution; cultures on blood-agar showed "dew-drop" colonies in twenty-four hours.

September 5. The patient had been comatose for several days, had vomited; emaciation had become marked. Râles were present throughout both lungs posteriorly. The head was retracted and back arched; Kernig's sign was marked; there was no Babinski's sign and no ankle clonus. Lumbar puncture at 3:30 p. m.: About 12 c.c. of turbid fluid obtained; numerous polymorphonuclear cells and Gram-negative bacilli; test for hexamethylenamin positive in 1 to 20 dilution; cultures showed "dew-drop" colonies on blood-agar in twenty-four hours. An attempt was made to fix the needle in the spinal canal and thus secure continuous drainage. Sterile dressings were placed about the needle and it was fixed with a split rubber tube, the tails being spread out over the skin and fastened down with adhesive plaster. Drainage seemed to be good at first and the dressings became wet through. The temperature fell just after lumbar puncture to 99.5 F.

September 6. The temperature remained normal all day. Retraction of the head and Kernig's sign persisted; there was marked priapism, probably due to hexamethylenamin; numerous râles were present throughout both lungs posteriorly. The urine was collected by absorbing it with cotton and squeezing it out; about 6 c.c. obtained. It was highly colored and contained a heavy trace of albumin. The guaiac and turpentine test for blood was positive, and a positive test for hexamethylenamin was obtained in a 1 to 75 dilution. During the afternoon the dressings over the needle left in the spinal canal were removed, and it was found that the needle had worked out and only the point was beneath the skin; drainage, of course, had ceased. An attempt to withdraw more fluid by lumbar puncture failed.

September 7. The temperature rose again during the night and remained high; the patient died at midnight.

Autopsy.—There was a thick greenish-yellow purulent exudate over the cord and base of the brain, extending upward in the sulci. The cortex, however, was not covered. The lateral ventricles were distended with turbid fluid. There was a fibrino-purulent exudate outside of the dura and extending into the lumbar tissues through which the needle passed when it was inserted for fixation. The middle ear on each side showed a thickened moist membrane. There was a small area of bronchopneumonia in the left lower lobe. Examination of the areas

4. The test is made as follows: To 2 or 3 c.c. of the fluid to be tested add one drop of 3 per cent. ferric chlorid and then a pinch of phenylhydrazin hydrochlorid. Place the test-tube in crushed ice and add about 1 c.c. of pure sulphuric acid. A delicate pink to a deep red color indicates a positive reaction. The color is brought out better by adding a drop or two of milk to the fluid before testing. We were able to obtain positive tests with a 1 to 1,000,000 dilution of formaldehyd and with a 1 to 75,000 dilution of hexamethylenamin. The reaction develops much more slowly with hexamethylenamin than with formaldehyd, but it can be hastened with the former by acidifying and just bringing it to the boiling point before making the test. This procedure rapidly decomposes the hexamethylenamin and liberates formaldehyd.

where hexamethylenamin was given intramuscularly showed no induration, hemorrhage or necrosis. Smears made from the cerebral meninges, the cord, the middle ears, and from the exudate in the lumbar region about the track of the needle all showed pus-cells and numerous small bacilli. Cultures from the cortical meninges and heart's-blood on blood-agar remained sterile. Cultures from the small area of bronchopneumonia showed several different types of colonies, among which were "dew-drop" colonies of small Gram-negative bacilli.

Bacteriologic Cultures.—Cultures made on blood-agar from the spinal fluid obtained September 1 and from the cerebral meninges and heart's-blood at autopsy were sterile. Cultures made on blood-agar from the spinal fluid obtained September 2, 3, 4, and 5 showed pure growths of small, discrete, "dew-drop" colonies, made up of small Gram-negative bacilli. Some of these grew in threads, and many gave the "safety-pin" appearance. These organisms failed to grow on plain agar and blood-serum, and the cultures died out in three days. Cultures made on blood-agar at autopsy from an area of bronchopneumonia showed typical small "dew-drop" colonies of small Gram-positive bacilli, associated with colonies of other organisms, among which were Gram-negative, lanceolate diplococci, probably pneumococci.

DISCUSSION OF CASES

Case 1 illustrates the ease with which *B. influenza* may be overlooked if one is not searching with it particularly in mind. The cases of influenzal meningitis have been so rare, or have been considered so rare, heretofore, that one's mind has not been alert to the possibility of a given case of meningitis being influenzal. Reports of cases have been so numerous within the past few years, however, that one is less likely now to overlook the organism. Case 1 is interesting also because in the beginning it simulated acute anterior poliomyelitis, and the differentiation was made only by lumbar puncture. The absence of retraction of the head, or even of marked stiffness of the neck, was unusual. Kernig's sign developed only one day before death, while Babinski's sign was present from the first. The exudate covering the entire brain and cord was the most massive that we have seen in any meningitis. Hexamethylenamin was given in heroic doses and was demonstrated in the spinal fluid by Hehner's test, but it appeared to have no effect on the course of the disease. However, its administration was begun rather late.

In Case 2, symptoms pointing toward meningitis did not appear until the sixth day. Hexamethylenamin was given in large doses by intramuscular injection, and was demonstrated in the spinal fluid diluted twenty times when the phenylhydrazin hydrochlorid test was used. Estimated by colorimetric methods, it was present in the spinal fluid in 1 to 3,750 solution, and in 1 to 1,000 solution in the urine. In the urine, however, it was probably partly decomposed and some formaldehyd was probably present. Priapism developed, possibly from drug irritation, and hemoglobin in the urine was demonstrated by the guaiac and turpentine test. This hemoglobin was probably due to hexamethylenamin hematuria. The sites of injection of hexamethylenamin showed no induration, hemorrhage, or necrosis, when examined at autopsy. (A 1 to 10

solution in normal salt was used for intramuscular injection.) Hexamethylenamin appeared to be without effect on the course of the disease until permanent drainage was begun, when the temperature fell to normal and remained normal for about twenty-four hours, when the drainage needle worked out and drainage ceased. We feel that the measure was used too late in this case to have saved the patient in any event, for the patient had become markedly emaciated and was almost moribund when drainage was begun. The effect on the temperature, however, leads us to believe that the combination of permanent drainage and hexamethylenamin may be of benefit in meningeal infections for which we have no serum. In a subsequent case of pneumococcus meningitis, Dr. Lloyd Noland kindly performed lumbar laminectomy for us, and we treated the patient with large doses of hexamethylenamin by intramuscular injection. The patient died within twenty-four hours and at autopsy it was discovered that the condition was complicated by pneumococcus endocarditis, which we had not diagnosticated during life. There was a large vegetation on the aortic valve and one of the cusps was almost perforated. The case was not, therefore, of experimental value.

Recently Rosenthal⁵ has described a special cannula for establishing permanent drainage of the spinal canal. He refers to Gorse, who maintained lumbar drainage for thirteen days in a case of suppurative meningitis, and whose patient recovered. Rosenthal has used permanent drainage in tuberculous meningitis and has noted an arrest of convulsions and diminution of pain. He does not include the use of hexamethylenamin in his treatment.

DISCUSSION OF THE LITERATURE

The most notable reviews of the literature of influenzal meningitis within the past few years have been those of Adams,⁶ Cohoe,⁷ Cohen⁸ and Wollstein.⁹ Wollstein gives the latest and fullest review of the literature and contributes eight additional cases. In her summary she includes among forty-nine well proved cases with pure cultures, a case reported by Davis¹⁰ that we think should be classed as only a possible case. Twins died on the ninth and twelfth days after birth. Autopsy on the first showed a purulent meningitis and *B. influenza* was isolated. There was no lumbar puncture or autopsy on the second twin. While the second twin had the same symptoms as the first and probably died from the same disease, still the case cannot be accepted in the proved class. On the other hand, one of Wollstein's own cases is omitted from the summary.

5. Rosenthal, G.: Bull. Soc. de pédiat. de Paris, October, 1910, No. 7, p. 401.

6. Adams, S. S.: Arch. Pediat., 1907, xxiv, 721.

7. Cohoe, B. A.: Am. Jour. Med. Sc., 1909, cxxxvii, 74.

8. Cohen: Ann. de l'Inst. Pasteur, 1909, xxiii, 273.

9. Wollstein, M.: Am. Jour. Dis. Child., 1911, i, 42.

10. Davis, D. J.: Arch. Int. Med., 1909, iv, 323.

This subtraction and addition leaves the number of cases collected by her at forty-nine. To these forty-nine cases should be added two cases reported by Hymanson¹¹ and five cases with one recovery reported by Batten.¹² In the latter's paper the bacteriologic reports are meager, but there is evidence that the criteria of identification of *B. influenza* were appreciated, and the writer states that pure cultures of *B. influenza* were obtained in each case. The patient that recovered was a child 14 months old and was treated with hexamethylenamin, 10 gr. every four hours. These seven cases and our two added to the forty-nine collected by Wollstein give a total of fifty-eight cases in all of which *B. influenza* was obtained in pure culture. Including Batten's case, there have been only six recoveries. Dunn¹³ mentions having encountered four cases of fatal influenzal meningitis, but he does not state whether *B. influenza* was identified by cultural characteristics or merely by stains of coverslip preparations made from the spinal fluid. We infer that the latter method only was used. The four cases mentioned in Holt's¹⁴ recent article we presume were the same as the four from the Babies' Hospital reported by Wollstein.

DIAGNOSIS

The diagnosis, of course, can be made during life only by lumbar puncture and by identification of the organism, while the latter to be conclusive must be accomplished by means of cultures. Stained smears of spinal fluid may furnish presumptive evidence that one is dealing with an influenzal meningitis, but there are other Gram-negative bacilli found rarely in spinal fluid, and morphology alone cannot be trusted for differentiation. Furthermore, there are certain chances of contamination which must be considered and which render stained specimens unreliable. For instance, some two years ago in two instances we used for collecting fluid from lumbar puncture test-tubes from which we had poured sterile bouillon. The spinal fluids seemed quite turbid and numerous Gram-negative bacilli were present. Transplants on various media yielded no growth, however, and we were puzzled for an explanation until we found that the organisms were dead bacilli that had settled to the bottom of the sterile bouillon and had remained in the test-tube when the bouillon was poured out. Again, more recently, convulsions and meningeal signs developed in a patient who suffered only from pneumonia, as autopsy subsequently proved. In fluid from lumbar puncture we found a slight increase in the number of cells and a few small bacilli in smears stained with a saturated aqueous solution of methylene-blue. We thought that

11. Hymanson, A.: New York Med. Jour., Dec 25, 1909.

12. Batten, F. E.: Lancet, London, 1910, i, 1677.

13. Dunn, C. H.: Am. Jour. Dis. Child., 1911, i, 95.

14. Holt, L. E.: Am. Jour. Dis. Child., 1911, i, 26.

we could find some Bismarck brown stained bacilli in the Gram preparations, but we were not sure. Cultures on blood-agar remained sterile. The patient presented such marked meningeal signs that we felt that meningitis must surely be present, and that our technic must have been faulty in that no growth was obtained in cultures. We relied, therefore, for a diagnosis on the symptoms and the methylene-blue stains, and were chagrined at autopsy when no meningitis was found. We then discovered that the methylene-blue stain was contaminated with a small Gram-negative bacillus. We have been troubled, also, by the growth in our Giemsa stain of a similar little bacillus which adheres to every preparation placed in the staining jar. Several years ago one of us (Brem) encountered a bipolar staining bacillus in a carbol fuchsin stain of material aspirated from an inguinal gland in a patient suspected of having plague. These organisms influenced us in arriving at a diagnosis but were afterward found to be contaminating bacilli in the carbol fuchsin.

BIOLOGICAL CONSIDERATIONS

The most extensive and important study of the biological properties of the influenza-like organism causing cerebrospinal meningitis has been made by Cohen,⁸ who was led by his researches to the conclusion that the organism of meningitis, although culturally like *B. influenza* of Pfeiffer, is in reality a different species, and he proposes that the meningitis caused by it shall be called septicemic cerebrospinal meningitis. Cohen drew his conclusions from numerous animal experiments, in which the pathogenicity and immunizing properties of his organism and Pfeiffer's were studied. He concluded from these and from serodiagnostic reactions, especially bactericidal properties of immune serum and conglutination tests, that the organisms were not identical. It may be worth while to review briefly the main experiments of his researches and the principal arguments that may be advanced in support of his view.

1. In agreement with Pfeiffer and others, he found that although rabbits could be killed by massive intravenous, but not by subcutaneous, doses of *B. influenza* the organisms could not be recovered from the heart's-blood (except in the case of a strain isolated by Bordet from a patient with whooping-cough). On the other hand, the bacillus of meningitis killed rabbits in relatively small doses given intravenously or subcutaneously and could invariably be recovered from the heart's-blood. Also that its virulence increased by passage through rabbits.

2. Immune serum against Pfeiffer's bacillus did not protect animals against the bacillus of meningitis, but immune serum against the latter organism protected animals and even cured them when given twenty-four hours after a subcutaneous lethal dose of the same bacillus.

3. Conglutination tests showed a very marked difference in the reactions when an immune serum against *B. influenza* was tested against the two organisms, and, again, when an immune serum against the bacillus of meningitis was tested against the two. The first serum agglutinated *B. influenza* markedly and the bacillus of meningitis slightly, while the contrary was the case with the second serum.

4. Isolation from the blood during life of the bacillus of meningitis and from the heart's-blood at autopsy has been accomplished by a number of investigators, and it seems fairly certain that this form of meningitis is always accompanied by a septicemia. On the other hand, Pfeiffer and his school concluded that *B. influenza* did not pass into the blood. This difference in the distribution of the two organisms is found to be, likewise, a phenomenon in experiments on animals. Wollstein⁹ writes:

We have had the opportunity of studying a large number of strains of influenza bacilli during the past two years, of which four only were found to be virulent for rabbits. It is, perhaps, significant that of these four virulent cultures, three were derived from the cerebrospinal fluid from cases of influenzal meningitis, and the fourth from the heart's-blood at autopsy in a child succumbing to pneumonia. We have endeavored, in many cases at the Babies' Hospital, to obtain the influenza bacillus from the blood of the heart at autopsy, but unsuccessfully except in the previous case mentioned until the cases of influenzal meningitis came under observation. In four cases of this infection, the influenza bacillus was obtained from the blood of the heart.

She cites the similar experience of Wohlwill, who examined many hundreds of autopsies with this point in view, and never secured the bacillus from the blood. These observations go to support Cohen's separation of the meningitis organism. However, one of Wollstein's strains was found not to be virulent for rabbits. She also reports that protection experiments on mice with immune goat-serum "left the animal alive whether its homologous culture or a meningeal strain were used."

Thursfield¹⁵ in a recent article reports two cases of continued fever during which an organism resembling culturally *B. influenza* was isolated from the blood of two adult male patients. There was no meningitis. One of these patients probably had an attack of influenza preceding the continued fever; the other, however, had no signs of influenza and the onset was with phlebitis of the leg. Bacilli of one of the cultures were injected subcutaneously into a mouse without producing illness. Thursfield discusses the occurrence of influenza-like bacilli and he is definitely inclined to accept the conclusions of Cohen. His final conclusion is as follows:

A consideration of the foregoing propositions renders it certain that we must in future recognize that the organisms hitherto described as *B. influenzae* are not all identical with it, but, like the streptococci, staphylococci and the coli-typhoid family, belong to a group the various members of which possess very different pathogenic powers.

15. Thursfield, H.: Quart. Jour. Med., 1910, iv, 7.

We ourselves think that Cohen, in his excellent article, has presented strong evidence in favor of separating the meningitis organism from *B. influenza*, and that a repetition of his work with other organisms of meningitis will demonstrate that his views are correct. We would advance the suggestion, however, that infection with this organism may not produce frequently a meningitis but that, in the majority of the infections, there may be a septicemia only, from which the patients often recover.

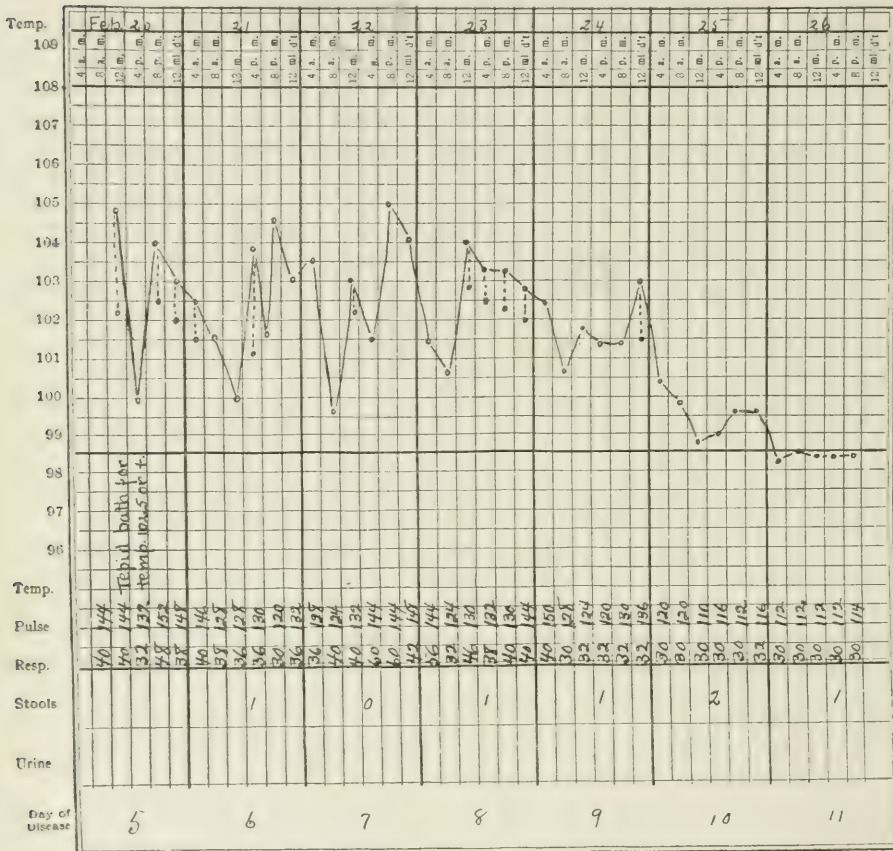


Chart 3.—Showing conditions in Case 3 (No. 29,851), a white American child 11 months old, admitted to Colon Hospital Feb. 20, 1911.

The pathogenic organism isolated from the heart's blood by Wollstein in the non-meningitic case, the organisms isolated in the two cases reported by Thursfield, the organism isolated from the blood by Slawyk and confirmed by Pfeiffer,¹⁶ the organisms isolated during life by Meunier from the blood of four children¹⁶ and the numerous influenza-like

16. Cited by Wollstein (see note 9).

organisms isolated from the heart's-blood by Hehle¹⁷ at autopsy on bodies of patients who had died of scarlet fever, measles, varicella, etc., all may belong, together with the meningitis bacillus, to a septicemic member of an *influenzoid group* of organisms, embracing not only Pfeiffer's bacillus and the meningitis organisms, but also the organisms of whooping-cough, the Koch-Weeks bacillus, the bacillus of Ducrey, the trachoma bacillus, and *B. catarrhalis*.

With blood-media introduced as routine in our blood-cultures, it would not be surprising to find that many of the undiagnosed fevers of childhood, some of the fevers of "gastroenteric intoxication," and other fevers of doubtful origin in children and adults were caused by this organism. In our work we have met with numerous instances of undiagnosed fevers (with negative blood cultures by transplants on ordinary media) which could readily be accounted for if such an hypothesis were proved to be correct.

As an illustration of this class of cases we present Chart 3, which gives the course of fever in a white American child, 11 months old.

CASE 3.—The child had been perfectly well previously and there was no sickness in the family. On the evening of Feb. 16, 1911, there was slight fever which day by day rose higher, with morning remissions, until February 20, when the child was brought to the hospital. Blood was examined once or twice daily for malarial parasites with negative results; a marked leukocytosis was noted in the slides and several counts ranged from 23,000 to 27,000 per c.mm. Two differential counts showed about the same percentages of leukocytes, polynuclear neutrophils 68.7, mononuclears and transitionals 12.8, small mononuclears 16.4, unclassified 2.1 per cent. February 18, two drops of blood from the ear were caught in bile-peptone. The medium remained sterile. The child did not have coryza, the throat and ears were normal, there were no abrasions on the skin, there was no bronchitis, the heart was normal, the spleen was not enlarged, no rose spots appeared, the stools were formed and perfectly digested, there were found no ova of parasites and no amebas. A second upper incisor tooth was about to appear, but there was no redness or swelling of the gum, and there seemed to be no pain. A slight internal squint developed in the left eye and continued into convalescence; and a Babinski reflex was constantly present. There were no other indications of meningeal involvement. The child remained in good condition throughout the nine days' illness. Several days after the temperature became normal, it rose again to 103 F. but fell to normal within twenty-four hours. One week later an apparent relapse occurred, and for four days the fever remained at a high level, 103 to 105 F. There was the same absence of signs and presence of a leukocytosis. The temperature fell rapidly to normal, and convalescence was uneventful.

The fever and leukocytosis give a picture of an acute infection. There were no signs indicating localized infection, and we feel inclined to believe that we were dealing with some form of septicemia. The case would fit well into a group with the cases in which Thursfield isolated influenza-like organisms. In his book Holt¹⁸ gives the chart of a case

17. Cited by Lord: Osler's Modern Medicine, ii, 481.

18. Holt, L. E.: Diseases of Infancy and Childhood. D. Appleton & Co., New York, 1903, p. 1113.

that he thinks was "uncomplicated influenza" with "no local signs of disease." The fever curve was very much like that of our Chart 3, except that the fluctuations were more marked. The duration of illness was ten days; in our case, nine.

We feel that there are probably a large number of cases that belong to this group, and that go unreported because physicians have been unable to classify them. It does not seem improbable to us that they, together with meningitis cases, are caused by a septicemic member of the *influenzoid group*. The whole matter is one of great interest and importance and affords an attractive field for further investigation.

SUMMARY

1. Two patients, 18 and 23 months old, respectively, with meningitis caused by a bacillus culturally like *B. influenza*, were treated with large doses of hexamethylenamin without apparent benefit. Both infections terminated fatally.

2. Late in the course of the disease in the second patient, while hexamethylenamin was being given, a needle was inserted into the spinal canal in the lumbar region and was left *in situ* in the hope of securing permanent drainage. Immediately afterward the temperature dropped practically to normal and remained normal for about twenty-four hours when it rose again. It was found that the needle had worked out and drainage had ceased.

3. The combination of permanent drainage and hexamethylenamin treatment may be of value in treating those cases of meningitis for which we have no specific treatment.

4. The literature on the subject of influenzal meningitis is discussed, and the biologic properties of the organism are considered.

5. The work of Cohen is reviewed in some detail, and the view is supported that in the bacillus of meningitis we are dealing with an organism not identical with Pfeiffer's, but one that is a septicemic member of an *influenzoid group*.

We wish to thank Col. W. C. Gorgas, chief sanitary officer, for permission to publish this paper.

THE DIAGNOSTIC VALUE OF A BLOOD EXAMINATION IN PERTUSSIS *

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Since Frölich's¹ studies of the blood in pertussis in 1897, numerous investigations have been made which show that decided and definite changes occur in the blood as a result of this disease. For the sake of brevity, no attempt will be made at this time to include a review of the literature, the reader being referred to an excellent article by Barach² and to my own report³ of twenty-seven cases, accompanied by a brief review of the literature and a full bibliography. More recently Donally⁴ has reported six cases in which leukocyte counts were made. He found a leukocytosis varying in degree from 9,300 on the third day of the disease to 62,000 during the paroxysmal stage. Ashby⁵ reported also, on examinations of the blood made in 100 cases. He considered leukocytosis itself, which ranged from 15,000 to 30,000 cells per c.c., a valuable aid in the diagnosis of suspicious cases. An increase in the lymphocytes was found in the catarrhal stage also, and in mild cases at all stages. His work, however, related chiefly to the total leukocytic content.

The blood formula in pertussis may be considered as fairly well defined. Early in the catarrhal stage there occurs a leukocytosis with an absolute increase in the percentage of small lymphocytes. The leukocytosis and lymphocytosis increase with the severity of the disease, reach their highest point in the paroxysmal stage and then fall by lysis, reaching normal proportions in from two to three months. In the stages of improvement a mild eosinophilia is found.

Whether one is justified in attempting to determine the degree of infectiousness of a given case by the blood findings, is questionable.

*From the Laboratory of the Philadelphia Hospital for Contagious Diseases.

*Read before the Philadelphia Pediatric Society, Dec. 13, 1910.

1. Frölich: Beitr. zur Pathologie des Keuchhustens, Jahrb. f. Kinderkr., 1897, xliv, 53.

2. Barach, J. H.: Morphology of the Blood in Pertussis, Arch. Int. Med., 1908, i, 602.

3. Kolmer, J. A.: Study of the Blood in Pertussis, Arch. Int. Med., 1909, iv, 81.

4. Donally, H. H.: Present knowledge of Whooping-Cough, Arch. Pediat., 1908, xxv, 819.

5. Ashby, H. T.: Diagnostic value of the Leukocytes Occurring in Whooping-Cough, Brit. Med. Jour., 1910, i, 1105.

Practically every one who has worked with the blood in pertussis has endeavored to determine whether the blood changes indicated occur early enough in the disease, and to a sufficient degree, to be of value in making a diagnosis before this is possible from the clinical symptoms. While the consensus of opinion has been in favor of this view, much more work is necessary to demonstrate the absolute reliability of the blood-findings.

When we consider the ravages and high mortality of whooping-cough, especially among the poor and in institutions for children, the assistance that such a method of diagnosis would render is at once apparent.

The disease is, without doubt, more contagious during the catarrhal stage, and since our known therapeutic measures are so ineffective, we naturally welcome a procedure that may result in the recognition of the disease in the pre-catarrhal stage, thus enabling us to isolate the infected at an earlier period, as well as to adopt other measures of prevention.

It is especially important to recognize pertussis early in the very young, among whom the mortality is strikingly high. Thus the figures of Johnson, quoted by Kerr,⁶ show a mortality of 35 per cent. in the first two years of life, 22 per cent. for the third year, 12 for the fourth, 8 for the fifth and 6 per cent. for the five- to ten-year period. The bacteriology of the disease is still too uncertain to be of any help in diagnosis. Even if the bacillus described by Bordet⁷ and Gengou⁸ was definitely proved to be the cause, the present day technic for isolating this organism and differentiating it from the other members of the influenza group of hemophilic bacilli to which it belongs consumes too much time to be of practical value.

It seems very important, therefore, since it appears probable that the blood examination may contribute something to the early recognition of pertussis, that studies along these lines should be undertaken whenever opportunity offers. With this object in mind the work herein reported was begun.

This paper has to do with a series of studies on (1) the diagnostic value of blood examinations in pertussis; (2) the modifying influence of scarlet fever on the blood-formula of pertussis.

Scarlet fever is, in itself, accompanied by changes in the blood. These consist essentially of a leukocytosis which occurs in the period of incubation, increases in proportion to the severity of the disease, and then begins to fall, usually after the first week or ten days. An absolute increased percentage of polymorphonuclear neutrophils accompanies this leukocytosis. The eosinophils are decreased with the onset of fever, they

6. Kerr, C. B.: *Text Book of Infectious Diseases*: Oxford Press, 1909, p. 463.

7. Bordet: *The Microbe of Whooping-Cough*. *Brit. Med. Jour.*, 1909, ii, 1062.

8. Wollstein, Martha: *The Bordet-Gengou Bacillus of Whooping-Cough*, *Jour. Exper. Med., Lancaster, Pa.*, 1909, xi, 41.

increase rapidly, reaching the maximum in the second or third week, after which they gradually decrease to normal.

All of the cases of pertussis considered in this paper complicated cases of scarlet fever.

Whooping-cough suddenly developed in a convalescent ward of the hospital during July, 1910, some patients having been admitted during the period of incubation. Since pertussis was quite prevalent throughout the city, every patient with scarlet fever admitted with a cough, was regarded as suspicious and isolated until a blood examination had been made. Likewise the blood of all patients developing cough after admission was subjected to examination. If the result of any of these examinations indicated pertussis, the patients were transferred to a special isolation ward, where they were detained for three days, when a second examination was made, which usually determined the diagnosis.

It may be well to emphasize the fact that considerable care must be exercised in making these examinations, to appreciate slight changes in the blood. The blood-picture differs according to age, a fact one must bear in mind in establishing a "normal" standard. The accompanying table (Table 1), which I composed after examining the blood of a large number of institutional children, is the normal which I have used for comparison:

TABLE 1.—SUMMARY OF BLOOD EXAMINATION OF NORMAL INSTITUTIONAL CHILDREN

Age, Years	Leuko- cytes	—Lymphocytes— Large Small		Transi- tionals	Poly- morpho- nuclears	Eosino- phils	Mast Cells
¼-1 ...	10,900	45.57	13.53	2.02	36.78	2.13	.07
1 -2 ...	11,600	41.55	13.86	1.53	42.66	1.45	.03
2 -3 ...	12,300	35.57	10.74	1.15	49.94	2.3	.01
3½-5 ...	10,800	27.62	9.06	.72	59.37	2.73	.15

The blood of forty-three patients was studied in this series. Total leukocyte and differential counts were made in each. Six were made late in the course of pertussis, and are of no interest from the standpoint of early diagnosis. Of the thirty-seven remaining, eleven were diagnosed as pertussis in the catarrhal stage by means of a blood examination, which diagnosis was later confirmed clinically; fifteen were given a negative diagnosis, none of which developed the disease; two were given a positive diagnosis, neither of which was confirmed clinically; three were diagnosed as negative, who later developed the disease; two were held as "suspicious" both of whom developed the disease; while four others, held as "suspicious," never had pertussis.

These results are tabulated below (Tables 2 to 8) in order to facilitate their rapid review. Since the modifying influence of scarlet fever was often difficult to eliminate, the stage of this disease at the time of the blood examination is indicated.

TABLE 2.—CASES IN WHICH A POSITIVE DIAGNOSIS OF PERTUSSIS WAS GIVEN
FROM THE BLOOD EXAMINATION. ALL OF THESE CASES PROVED
TO BE PERTUSSIS

Case Number	Name	Age, Years	Coughing Days	Leuko- cytes	—Lymphocytes— Small Large	Trans- tional	Poly- morpho- nuclears	Eosino- phils	Mast Cells	Stage of Scarlet Fever
2	G. T.	2½	6	16,000	50.95	19.1	3.82	25.47	.62	Third week, desquamating
7	J. H.	7	5	17,200	31.87	6.25	.62	59.37	1.87	2½ weeks slight desquamation
8	I. S.	3¼	3	10,000	41.83	6.56	.83	40.83	10.	3 months, free of desquamation
14	R. Z.	2	4	19,000	56.	3.	1.	38.	2.	3 months, free of desquamation
15	E. K.	2	2	9,000	50.	5.	3.	40.	2.	3 months, free of desquamation
21	C. G.	2	7	10,200	50.	6.	1.	38.	3.	6 weeks, slight desquamation
24	I. P.	6	5	11,000	54.	12.	1.	33.	0	5 weeks slight desquamation
25	M. G.	7	3	13,000	43.	1.	1.	52.	2.	Third day, moderate rash
28	L. C.	1½	6	11,600	58.	7.	1.	33.	1.	Fifth week, free of desquama- tion
29	R. F.	1	3	11,600	58.72	5.08	2.36	21.8	1.42	Tenth week, free of desquama- tion

TABLE 3.—CASES IN WHICH A NEGATIVE DIAGNOSIS OF PERTUSSIS WAS GIVEN FROM THE BLOOD-EXAMINATION. NONE OF THESE PATIENTS DEVELOPED PERTUSSIS

Case Number	Name	Age, Years	Days Coughing	Leukocytosis	Lymphocytes— Small Large	Transi- tionals	Poly- morpho- nuclears	Eosino- phils	Mast Cells	Stage of Scarlet Fever
1	H. R.	2½	4	10,000	20.83	1.66	50.	15.83	1.66	Second day, "intestinal rash"
3	L. W.	4	3	16,000	10.	3.	75.	41.	0	Second day, intense rash
4	W. D.	13	3	11,000	18.82	4.11	50.	23.36	59.	Seventh day, rash fading
9	M. T.	1½	3	11,000	34.71	10.71	49.	2.8	.71	Fourth week, slight desquama- tion
10	M. R.	4	2	11,000	35.	12.	46.	4.	0	Scarlet fever following burns of body
11	W. S.	1½	1	14,000	37.	8.	50.	1.	0	Sixth day, rash fading
12	A. M.	2	3	10,000	27.	15.	55.	1.	0	Slight rash
13	G. S.	3	3	15,000	35.	14.	53.	4.	.1	Third day, moderate rash
19	E. L.	3	3	18,000	14.	5.	77.	3.	0	Moderate rash
20	E. D.	5	5	10,500	33.	9.	55.	2.	0	Eighth week, free of desquama- tion
23	E. M.	4	3	17,000	12.	3.5	76.	5.	.5	Moderate rash
30	H. R.	5	2	9,000	24.	6.	65.5	1.	.5	Free of desquamation
33	K. K.	7	2	16,000	28.24	5.08	64.96	1.13	0	Second day, marked rash
36	E. P.	4	3	10,000	21.54	6.7	67.17	1.22	0	Moderate rash
37	F. W.	5	3	9,000	26.	12.	54.	5.	0	Slight desquamation

TABLE 4.—CASES IN WHICH A POSITIVE DIAGNOSIS OF PERTUSSIS WAS GIVEN FROM THE BLOOD-EXAMINATION. THESE PATIENTS DID NOT DEVELOP PERTUSSIS

Case Number	Name	Age, Years	Days Coughing	Leukocytosis	Lymphocytes— Small Large	Transi- tionals	Poly- morpho- nuclears	Eosino- phils	Mast Cells	Stage of Scarlet Fever
27	A. L.	8	1	7,500	43.	7.	44.5	2.5	0	Free of desquamation
31	A. McM.	5	1	18,000	40.	9.	44.	4.5	.5	Free of desquamation
31	12 days later...		..	12,000	33.	8.5	51.4	6.	.05	Not coughing

TABLE 5.—CASES IN WHICH A NEGATIVE DIAGNOSIS OF PERTUSSIS WAS GIVEN
FROM THE FIRST BLOOD-EXAMINATION. THESE PATIENTS
DEVELOPED PERTUSSIS

Case Number	Name	Age, Years	Days Coughing	Leukocytes	Lymphocytes— Small Large	Transi- tionals	Poly- morpho- nuclears	Eosino- phils	Mast Cells	Stage of Scarlet Fever
6	M. McD.	 6	6	18,000	15.	6.	1.	60.	18.	Ninth day, rash fading
6	9 days later	...	15	20,400	22.	1.	1.	73.	3.	
16	E. P.	 2	3	20,000	28.	3.	1.3	68.1	0	Seventh day, rash fading
16	3 days later	...	6	21,000	38.	9.	2.	49.	3.	Coughing hard
32	T. C.	 5	8	13,000	27.66	7.	3.66	55.64	.45	Twelfth day, desquamating
32	7 days later	...	15	14,000	52.5	8.	3.	36.	6.	Coughing hard

TABLE 6.—CASES IN WHICH A "SUSPICIOUS" DIAGNOSIS OF PERTUSSIS WAS GIVEN
FROM THE BLOOD-EXAMINATION. THESE PATIENTS SUBSEQUENTLY
DEVELOPED PERTUSSIS

Number	Name	Age, Years	Days Coughing	Leukocytes	Lymphocytes— Small Large	Transi- tionals	Poly- morpho- nuclears	Eosino- phils	Mast Cells	Stages of Scarlet Fever
35	E. H.	 7	4	10,000	39.	7.	1.5	58.5	3.	Sixth day, rash fading
35	10 days later	...	14	10,000	44.11	11.17	2.94	38.23	3.52	Coughing hard
26	M. S.	 6	3	9,000	28.5	13.	3.5	50.5	4.	Free of desquamation
26	5 days later	...	8	9,500	47.	11.17	2.8	32.35	7.	Coughing hard

TABLE 7.—CASES IN WHICH A "SUSPICIOUS DIAGNOSIS" OF PERTUSSIS WAS GIVEN FROM THE BLOOD-EXAMINATION. THESE PATIENTS DID NOT DEVELOP PERTUSSIS

Case Number	Name	Age, Years	Days Coughing	Leuko-cytes	—Lymphocytes— Small Large	Transi-tionals	Poly-morpho-nuclears	Eosino-philis	Mast Cells	Stage of Scarlet Fever
18	M. K.	 6	3	7,000	37.	7.	1.	54.	.5	Sixteenth day, slight desquamation
22	A. M.	 2	8	22,000	35.55	12.22	2.59	48.37	.74	Twelfth day, desquamating
38	E. C.	 6	4	11,000	32.11	4.5	1.5	59.39	.5	Eighth day, desquamating
43	S. F.	 2	2	11,000	44.44	11.11	3.33	37.77	0	Seventh day, rash fading

TABLE 8.—CASES IN WHICH A BLOOD-EXAMINATION WAS MADE LATE IN THE COURSE OF PERTUSSIS

Case Number	Name	Age, Years	Duration of Cough, Weeks	Leuko-cytes	—Lymphocytes— Small Large	Transi-tionals	Poly-morpho-nuclears	Eosino-philis	Mast Cells	Stages of Scarlet Fever
5	H. D.	 7	2½	19,800	46.66	7.33	.66	42.	0	Fifth week, improvement in pertussis
5	10 days later	...	...	12,000	20.	8.	1.	69.	0	Second day, mild rash. Paroxysmal stage of pertussis
34	A. K.	 3	4	24,800	66.	3.51	.64	26.64	0	Free of desquamation; marked improvement in pertussis
34	10 days later	...	...	16,800	60.	13.	1.	24.	1.	Slight desquamation. Improvement in pertussis.
39	J. S.	 2	6	11,900	36.	8.	.8	34.	0	Slight desquamation. Improvement in pertussis.
39	10 days later	...	...	10,800	32.	12.	2.	43.	0	ment in pertussis
40	J. D.	 6	5	12,900	50.	8.5	2.	36.5	0	Slight rash. Improvement in pertussis
40	7 days later	...	...	10,000	38.31	9.72	1.77	43.98	0	
41	M. G.	 4½	8	16,000	37.	8.	0	52.	0	
42	M. C.	 5	2½	25,000	39.03	5.16	.64	51.28	0	
42	10 days later	...	...	15,800	33.	12.	2.	49.	0	

All of these patients were convalescent scarlet fever patients except Case 25 (Table 2), in which the patient was coughing on admission. Since most of them were well along in convalescence from scarlet fever, the leukocytosis and increased percentage of small lymphocytes were accepted as sufficient evidence for the diagnosis of pertussis. The eosinophilia of scarlet fever was quite mild, save in Case 8, and since this child was so far along in convalescence the eosinophilia probably had some other origin.

Most of these patients were coughing on admission, and were held in isolation as suspicious. On account of the high leukocytosis which occurs in the acme of scarlet fever, it was frequently a difficult matter to state an opinion, and a diagnosis was possible only after careful consideration of the degree of severity of the scarlatina. It is interesting to note the more marked eosinophilia in many of these early cases.

In both of these cases the diagnosis was largely made on the presence of lymphocytosis. In Case 27 (Table 4) the patient coughed at night, followed by vomiting, but never whooped. In Case 31 the patient coughed hard for a week and then gradually grew better. Since this child was 8 years of age, it is a question whether this was not a genuine but mild case of pertussis.

Negative diagnoses were given in all at the first examination, on account of the low lymphocyte count, the leukocytosis being ascribed to the scarlet fever. The second counts are given to show the increasing lymphocytosis. Had we paused to estimate the total number of each leukocytic element in a cubic millimeter of blood, a negative diagnosis would not have been given to at least one of these cases, Case 6 (Table 5). For instance, if 9,000 leukocytes, and 27 per cent. small lymphocytes is normal for a child 6 years of age, this would mean that each c.c. of blood contained 2,430 of these cells. This case gave a leukocytosis of 18,000 with 15 per cent. small lymphocytes, which means 3,700 of these cells in each c.c. or an increase of 1,270 cells of this variety above the normal. Likewise Case 16 showed an increase of 1,090 and Case 32 an increase of 888 small lymphocytes per c.c. of blood above normal.

Both of these cases were held as "suspicious" on account of the lymphocytosis. The leukocytes in Case 35 (Table 6) could be accounted for by the scarlet fever.

In Case 18 (Table 7) the patient coughed a great deal at night; in Case 22 the patient had a severe pneumococcic angina and coughed hard but never whooped; in Case 38 the patient coughed hard for a week or so and then cleared up; in Case 43 the patient coughed considerably at night for five or six days and then gradually grew better.

These cases show the high leukocytosis and lymphocytosis in the paroxysmal stage, with a gradual decrease toward the stage of improvement when the cough is paroxysmal but without the whoop. In two cases, 39

and 40 (Table 8), the eosinophilia of scarlet fever was present, aided probably by the tendency toward an eosinophilia in the terminal stage of pertussis.

SUMMARY

1. Out of thirty-seven cases of cough which could not be diagnosed clinically from pertussis in the catarrhal stage, sixteen proved later to be pertussis. Of these, thirteen, or 81.25 per cent., had been diagnosed correctly by means of the blood examination. Three, or 18.75 per cent., were given an incorrect diagnosis. Of the twenty-one cases proving not to be pertussis, fifteen, or 71.4 per cent., were given the correct, and six, or 28.6 per cent., the incorrect diagnosis.

2. The presence of secondary infection which may by itself produce a leukocytosis with a relative or actual decrease of the small lymphocytes, will lead to error. In such cases it is better to be guided by the total number of leukocytic elements in a c.c. of blood rather than by percentages. We believe that, in the absence of a second infection, as scarlet fever in these cases, the percentage of error would have been less.

I wish to express my thanks to Dr. S. S. Woody, chief resident physician of the Philadelphia Hospital for Contagious Diseases, and Drs. Hull, Nicholson and Bowker, assistant resident physicians, for aid in the clinical observations of the cases and for their kind interest.

PROGRESS IN PEDIATRICS

BACTERIOLOGY AND PATHOLOGY

Does the Human Thymus Produce Blood-Cells?

(Johann Löw: *Wien. klin. Wchnschr.*, 1911, xxiv, No. 12, p. 418)

Löw has examined fifty-seven thymus glands, eight from the fetus, ten from new-born infants, thirty from children under 10, five from individuals between 11 and 20 years old and four from persons over 20 years of age. The cause of death was scarlet fever in four, diphtheria in five, pneumonia in one, sepsis in three, tuberculosis in six, hereditary syphilis in two, chronic eczema in one, enteritis in three, incarcerated hernia in one, cardiac anomalies in three, cerebral hemorrhage in one, burns in three, phosphorus poisoning in one, carbon monoxid poisoning in one, gunshot wound in one, status lymphaticus in two and Addison's disease in one. In all the thymus glands examined mononuclear and polynuclear eosinophils were found, more numerous in young children than in older individuals. Very few mononuclear neutrophils were found in the majority of the glands, though they were numerous in those patients dying of an infectious disease. No nucleated reds were found at all, and neutrophilic myelocytes were very rare, except in infections. Löw concludes that his researches show that the thymus gland takes no part in the production of blood-cells in extrauterine life.

MAURICE OSTHEIMER.

Blood-Pressure in Children

(V. Salle: *Jahrb. f. Kinderh.*, 1911, xxiii, No. 3)

The investigations undertaken by Salle were made on normal children from three to eleven years of age and on children suffering from a variety of disturbances. He found that the minimum and maximum blood-pressure rises with the age of the child, and that to a certain extent is dependent on the weight and size of the child. Variations from the average were noted in cases of lymphatism (the pressure being lowered) and in neuropathic cases and nephritis (the blood-pressure being higher).

F. C. Z.

Bacterial Count of Separator Cream and Separator Milk

(P. G. Heinemann and E. E. Class: *Jour. Am. Pub. Health Assn.*, 1911, i, 209)

Experiments were undertaken to determine whether the amount of fat in the cream bore any relation to the bacterial content and whether a definite relation could be established with the bacterial count of the separator milk. Dilutions of whole milk, cream and separator milk were plated in 1 per cent. glucose-agar of 1 per cent. acidity to phenolphthalein, incubated at 20 C. and the colonies counted after three days. It was found that separator cream contains smaller numbers of bacteria than the milk from which it is obtained and the number decreases proportionately as the fat content increases. The number of bacteria in separator milk is larger than the number in the milk from which it is obtained if the cream contains up to about 38 per cent. fat, and the number decreases proportionately with the increase of fat in the separator cream.

RICHARD M. SMITH.

METABOLISM AND NUTRITION

The Sugar Content in the Blood of Nurslings

(S. Cobliner: *Ztschr. f. Kinderh.*, Dec. 22, 1910, i, No. 3)

It is a well known fact that some nurslings suffering from nutritional disturbances sometimes eliminate sugar in the urine. The author directed his observations to finding out whether nurslings who eliminated lactose, saccharose and galactose also had an increased sugar content in the blood. The blood used for examination was removed from the back beneath the scapula by means of a wet cup. A sufficient quantity is easily obtained by this means. Seven infants, from nine to twenty-one days old, gave an average of about .08 per cent. of sugar in the blood. Those from one to twelve months of age gave an average of about .12 per cent., the lowest being .09 per cent. and the highest .15 per cent. These figures show that the nursling has a much higher blood sugar content than the adult; in fact, if the adult gave the same percentages of sugar in the blood the condition would be regarded as one of hyperglycemia. In none of these cases was Cobliner able to find any sugar in the urine. The observations were made under similar conditions. Further, he found that the sugar content of the plasma was higher than that of the blood as a whole. In fourteen cases the plasma sugar content was .126 per cent. To account for the increased amount of sugar in the blood in the infant, the author calls attention to the fact that naturally the nursling consumes large quantities of milk-sugar and, inasmuch as this is effectively taken care of by the economy, the healthy infant would not eliminate any of this sugar in the urine, thus accounting for the latter finding. Children in whom the sugar content in the blood is remarkably high are those presenting an exudative diathesis. In the case of six children, Cobliner found .15 per cent. sugar in two, and .166 per cent., .173 per cent., .1875 per cent. and .225 per cent., respectively, in the remaining four. No sugar was found in the urine of any of these children. In cases of tetany, these findings were negative. All these observations were made on normal children, except where otherwise stated. In the case of children suffering from sugar dyspepsia and intoxications, the amount of sugar varied in the case of six infants examined from .094 per cent to .123 per cent. Thus, it is evident that in these conditions the sugar content is not increased. In several cases in which the sugar content was estimated during the reparative stage, Cobliner found the same high percentages as in the acute stage. If sugar is found in the urine in these cases, it is probably because of the fact that the kidney is throwing out the sugar which has found its way into the circulation because of the pathologic condition of the intestinal wall. In the case of infants suffering from putrefactive intestinal disturbances, the sugar content is considerably lower than in the case of the adult. It varied in the cases of nine patients examined from .04 per cent. to .135 per cent. During the convalescent period the sugar content increased in amount with the continued improvement of the child until it finally reached the normal. Cobliner is of the opinion that in the case of atrophic infants the decreased sugar content is probably due to an error in liver function. This belief is borne out by the findings of Pfaundler and others. In infants in whom fever was produced by means of the administration of table salt Cobliner found hyperglycemia, and also, in a few instances, glycosuria. These findings are accounted for on the basis of the effect which large quantities of salt would have on the kidney. All this work shows that nurslings normally have a much greater sugar content in the blood than adults; that in cases of exudative diathesis there is a hyperglycemia; that in dyspepsias and intoxications the blood sugar content is not increased; that in cases of decomposition or putrefactive disturbances in the intestines there is a hypoglycemia which gradually reaches the normal as the patient's condition improves. Finally, in the so-called cases of "salt fever" there may be a hyperglycemia.

F. C. Z.

The Action of Various Sugars in the Nutritional Disturbances of Nurslings

(J. S. Leopold: *Ztschr. f. Kinderh.*, Dec. 22, 1910, i, No. 3)

The author endeavored to determine the relationship between various sugars and bowel disturbances, influence on the body-weight and temperature-curve. He made use of chemically pure lactose, saccharose, maltose, glyucose, Soxhlet's *naehr-zucker* and Loefflund's *naehrmaltose*. Thirteen infants were selected in whom there was a known nutritional disturbance, although no symptoms were noted at the time. The sugar was administered in 15 to 30 gm. doses, each dose being given in solution in 100 c.c. of distilled water. The sugar was administered in the evening between two feedings. The temperature was taken every two hours and the child was weighed daily at a given time. The children were fed with buttermilk to which the sugar was added, or, with half milk and about 4 per cent. of "flour-malt-soup-extract," or, a mixture of mother's milk and buttermilk. In the main, Leopold's findings confirmed those of other observers. Pure sugar caused bowel disturbances in 50 per cent. of the buttermilk-fed children and in 66 per cent. of the half-milk, malt-soup-fed-children. As regards weight, of fifteen children, who had normal stools, and following the administration of the sugar, developed a diarrhea, four lost in weight and eleven gained in weight. Of fifty children suffering from a slight bowel disturbance when the experiment was begun twenty-three lost in weight and twenty-seven gained. There did not appear to be a definite finding with regard to loss or gain in weight in any of these cases. Sometimes there was a marked loss of weight in the case of children suffering from a very mild form of diarrhea, while, on the other hand, in severe cases there was a decided gain in weight; while in still other cases no change was noted. The amount of sugar given did not always produce similar results nor did it appear to have any stated or dependable action in all cases. The author thinks it possible that the salt content has some bearing in this direction. In 110 instances, the effect of sugar on the temperature curve was noted. Leopold found that elevation of temperature occurred more often following the administration of dextrin-maltose containing carbohydrates than in the case of pure sugar. The condition of the bowel mucosa also has a bearing on these findings. In no case was there any elevation of temperature when the stools remained normal. Only when there was diarrhea was fever observed. However, that was not true of every case of diarrhea. For instance, in twenty-nine cases of diarrhea following the administration of milk-sugar fever occurred only fifteen times, so that something more than diarrhea and the resultant bowel condition is necessary to produce fever. Of thirty-five children fed with buttermilk and mixtures of buttermilk and mother's milk—mixtures rich in whey—eighteen, or nearly 50 per cent., showed elevation of temperature after the administration of a single dose of sugar. Of forty-five children fed with mixtures deficient in whey, thirteen, or 30 per cent., developed fever; therefore, it may be concluded—if so small a number of cases warrants a conclusion—that "sugar fever" occurs more often following the feeding of mixtures rich in whey than otherwise. The amount of sugar given did not seem to have any bearing on this question. The temperature curve in "sugar fever" was exceedingly variable. In a considerable number of cases it was like the temperature curve of "salt fever"; that is, the temperature rose shortly after the ingestion of the sugar, reaching its maximum in from four to six hours, and then defervescing. In other cases the reaction was delayed, sometimes as long as twenty-four hours. Occasionally, there was noted a febrile condition extending over several days, accompanied by loss of weight and evidences of illness on the part of the infant. No relation between the height of the fever and the status of body weight was noted. On the whole, Leopold says that the dextrin-maltose mixtures when administered in a single dose of from 10 to 30 gm. produce less diarrhea and less fever than pure sugar. Milk-

sugar, on the other hand, stands at the other extreme in that it is the most likely to produce diarrhea and fever. The opposite is true of saccharose. Further, the production of the so-called "sugar fever" depends not only on the kind of sugar given, but on the condition of the bowel and the nature of its contents. Mixtures rich in whey are more likely to produce febrile reactions than mixtures containing little whey. The temperature curve of "sugar fever" differs from that of "salt fever" in that the elevation occurs later, probably because bowel disturbances occur later.

F. C. Z.

ACUTE INFECTIOUS DISEASES

A Skin Eruption in Six Consecutive Cases of Poliomyelitis

(A. G. Brown: *Pediatrics*, *xxiii*, No. 4)

Brown describes skin eruptions in poliomyelitis as follows: The character of the rash was fairly uniform, and the distribution seems to vary little. In all cases it appears as a small papule, quite shot-like in character, with a tiny inflammatory base. This may or may not go to vesiculation. If it does, the vesicle is about the size of a pin-head, and looks not unlike a small chicken-pock, containing a clear fluid. The vesicle is quite hard and those papules which terminate in a vesicle lose their inflammatory base. The rash may appear in all stages on the same patient. The distribution is indefinite, but in all cases the papules are most abundant on the paralyzed limbs. They do not appear to follow any definite nerve-segments nor are they painful to the touch. The smears and cultures from the serum of the vesicles have shown no uniform results, while the sections through the vesicles show them to be only superficial.

HENRY F. KEEVER.

Biologic Differences Between Streptococci of Septicemia and Scarlet Fever

(F. Schleissner and W. Spaet: *Jahrb. f. Kinderh.*, 1911, *xxiii*, No. 3)

Following out the work of other observers, the authors endeavored to determine whether there existed any biologic differences between the streptococci found in septicemic conditions and those believed by some to be the cause of scarlet fever. The measure of differentiation was the action of rabbit's leukocytes on the organism. The method employed was similar to that of Weil and Toyosumi. The leukocytes were obtained by injecting aleuranot emulsion into the pleural and peritoneal cavities. The streptococci were, in most instances, obtained directly from the blood. The leukocyte masses were collected in glass tubes, each containing about 0.15 gm. When ready for use 1 c.c. blood-serum mixed with agar was added to each tube and plated. Later 1 c.c. of defibrinated rabbit's blood was added in place of the serum. When inactivated serum was added to the tubes the results varied. In the case of some strains of streptococci, growth was retarded, while in others it was promoted. Even with the same strains, variable results were obtained. It was definitely determined, however, that the so-called septic streptococci differed in the reactions obtained by this method from the scarlet fever streptococci, although the authors are not prepared to put forward or claim any etiologic relationship between these streptococci and scarlet fever. The various streptococci used in the experiments are simply regarded as different strains of the same organism. It is interesting to note that the scarlet fever streptococci were almost uniformly killed when leukocytes and active serum were used in the experiment. In these cases, other streptococci flourished as usual. It is believed by the authors, however, that if any attempt is made to produce a scarlet fever serum this must be made from organisms obtained from the blood of scarlet fever patients.

F. C. Z.

A Collected Study of Sixty Cases of Meningitis and Conditions Simulating Meningitis, with Special Reference to Diagnosis

(A. Sophian: *Arch. Pediat.*, March, 1911, *xxviii*, 201)

The author from a clinical and bacteriologic study of sixty cases of meningitis and conditions simulating it, concludes that a true etiologic diagnosis is difficult in private practice. Tuberculous meningitis is the most common form and at times very difficult to differentiate from epidemic cerebrospinal meningitis. It is most common in children under 2 years of age. Of this disease the slow onset, stupor, transient localized paralyses, irregular pulse and breathing, low temperature, inconstant reflex signs, and vasomotor changes are characteristic. In epidemic cerebrospinal meningitis the subjects are older, onset acute, temperature high and intermittent, vomiting projectile, irritability and delirium marked, reflexes irregular and palsies often absent. The symptoms most characteristic of these two forms may be present together and make diagnosis difficult. Diagnosis of meningitis due to other organisms can be made only by lumbar puncture. Clinically they resemble the cerebrospinal form. The spinal fluid may be sterile although a localized cortical meningitis be present. Bronchopneumonia simulates meningitis more frequently than other acute infection. The meningeal symptoms accompanying acute general infections can with care be differentiated from true meningitis. Poliomyelitis and polio-encephalitis may simulate the early stages of meningitis. The higher blood-count in the latter aids in diagnosis. Immediate planting of spinal fluid in culture media is necessary because of the tendency to rapid autolysis. The media used were 2 per cent. glucose-serum-agar, or bouillon, and blood-agar. In tuberculous meningitis the bacilli are easily found in the clot or by centrifuging. They are easily demonstrated in fluid taken post-mortem. The gross increase in fibrin content and cyto-count also aid in diagnosis. Fehling's reduction test was found uncertain. The globulin test of Noguchi was confirmed in a few cases so examined.

H. B. WILCOX.

The Value of Lumbar Puncture and the Leukocyte Count in the Diagnosis of Acute Poliomyelo-Encephalitis (Infantile Paralysis)

(John Lovett Morse: *Arch. Pediat.*, 1911, *xxviii*, 164)

Morse believes that it seems safe to conclude from present data that during the acute stage of acute poliomyelo-encephalitis the cerebrospinal fluid is clear and not infrequently under somewhat increased pressure; that it often shows a fibrin clot, which may persist for two or three weeks and perhaps longer; that it always contains an excess of cells; that these cells are chiefly of the mononuclear type, most of them being lymphocytes; and that these changes are present before the appearance of the paralysis. These changes are, however, identical with those found in tuberculous meningitis, the disease with which it is perhaps most likely to be confounded. It is true, of course, that the cerebrospinal fluid in tuberculous meningitis contains tubercle bacilli. They are missed in about 90 per cent. of the cases, however, if the examination is the usual routine one. If tubercle bacilli are found in the cerebrospinal fluid, the diagnosis of tuberculous meningitis is, of course, positive; if they are not found, the examination of the fluid is of no assistance in the diagnosis between tuberculous meningitis and acute poliomyelo-encephalitis. The characteristics of the cerebrospinal fluid in the early stage of acute poliomyelo-encephalitis are so different from those in the early stage of cerebrospinal meningitis—in which the fluid is turbid or purulent, contains a large number of polynuclear cells, and, as a rule, numerous meningococci—that there is no possibility of confusing them. Lumbar puncture is, therefore, of the greatest assistance in differentiating between these two conditions. It is of equal value in distinguishing acute poliomyelo-encephalitis from influenzal and pneumococcal meningitis and from the meningitides due to the pus organisms. The changes in the cerebrospinal fluid in the early stage of acute poliomyelo-

encephalitis are so definite that when they are found it is possible to exclude all diseases outside of the meningitides. Lumbar puncture, therefore, provides a most valuable means of diagnosis in this disease. Unfortunately, there is nothing whatever characteristic about the early symptoms of acute poliomyelo-encephalitis and in order to recognize the disease early, before the onset of the paralysis, at a time when treatment might possibly be of some value, it would be necessary to do a lumbar puncture on every sick child. This hardly seems a rational procedure. Treatment can do no good after the appearance of the paralysis, because the harm is then already done. Lumbar puncture at this time simply makes possible the verification of the clinical diagnosis. The value of lumbar puncture in the early diagnosis of acute poliomyelo-encephalitis is, therefore, very limited, in spite of the marked changes in the cerebrospinal fluid in the disease. Morse regards the leukocyte count as of little or no assistance in the early diagnosis of acute poliomyelo-encephalitis. There is at present not sufficient evidence to show whether or not there is a relative or absolute lymphocytosis in the early stages.

F. C. Z.

TUBERCULOSIS AND SYPHILIS

Fourth Complete Summary of the Arbeits and Teachings of Tuberculosis (1909)
(H. Schelble, Freiburg: *Monatschr. f. Kinderh.*, original, 1911, ix, 563)

MONOGRAPHS AND CONGRESSES

1. Bandelier and Roepke: Lehrbuch der speziellen Diagnostik und Therapie der Tuberkulose (A. Stuber, Würzburg).
2. Bandelier: Die Verhütung und Bekämpfung der Tuberkulose als Volkskrankheit (A. Stuber, Würzburg).
3. Bartel: Probleme der Tuberkulosefrage (F. Deuticke, Wien).
4. Engel and Bauer: Klinische und experimentelle Studien zur Pathologie und Therapie der Tuberkulose im Kindersalter (A. Stuber, Würzburg).
5. Hamburger, F.: Allgemeine Pathologie und Diagnostik der Kindertuberkulose (F. Deuticke, Wien).
6. Jessner, S.: Hauttuberkulose (A. Stuber, Würzburg).
7. Kirchner, M.: Die Tuberkulose in der Schule (A. Schoetz, Berlin).
8. Fifth Annual Report of the Henry Phipps Institute, February, 1907-February, 1908 (Phipps Inst., Philadelphia).
9. Roth, E.: Gesundheitsregeln für die Schuljugend (A. Schoetz, Berlin).
10. Sahli, H.: Tuberkulinbehandlung und Tuberkuloseimmunität (Schwabe & Co., Basel, 1910).

The monographs 1 to 9 have been reviewed in the *Monatschrift für Kinderheilkunde*, ix, part 1, in the "Referat."

The third revised edition of Sahli's writings handles the principles, technic, indications and results of tuberculin treatment; no physician should begin treatment with tuberculin without having previously studied this volume. The theoretical part is also worth reading and especially the part on Scrofula for the Pediatricist. Sahli's conception of the nature of scrofula coincides in the main with that of most modern pediatricians, but does not touch on one important factor as a cause of scrofula; i. e., on the harmful effects of over-feeding.

A. STATISTICS AND DISSEMINATION

11. Aronade, O.: Die Tuberkulose des Säuglings, *Ergebn. d. inn. Medizin und Kinderh.*, iv.
12. Beitzke, H.: Ueber die Häufigkeit der Tuberkulose am Leichenmaterial des Berliner pathologischen Institutes, *Berl. klin. Wchnschr.*, 1909, p. 389.
13. Fränkel, B.: Weitere Mitteilungen zur Abnahme der Tuberkulosesterblichkeit, *Berl. klin. Wchnschr.*, 1909, p. 2010.
14. Franz: Ergebnisse mehrjähriger Beobachtungen an tausend im Jahre 1901 und 1902 mit Tuberkulin zum diagnostischen Zweck injizierten Soldaten, VIII intern. Tuberkulosenkonferenz, 1909.
15. Gottstein, A.: Ueber die Abnahme der Tuberkulosesterblichkeit, *Berl. klin. Wchnschr.*, 1909, p. 2138.
16. Hamburger, F.: Die Tuberkulosehäufigkeit im Kindersalter, München. med. Wchnschr., 1909, p. 449.
17. Hamburger: Die Tuberkulose als Kinderkrankheit, München. med. Wchnschr., 1909, p. 462.

18. Hillenberg: Zur Entstehung und Verbreitung der Tuberkulose, *Ztschr. f. Hyg.*, lxi, 305.

19. Karlsson, S.: Untersuchungen über die Häufigkeit der Lungenschwindsucht in den Elementarschulen in Stockholm, VIII intern. Tuberkulosekonferenz.

20. Saugmann, Chr.: Die Tuberkulosefrage in Dänemark, 1908, *Ztschr. f. Tuberk.*, 1909, p. 219.

21. Schlossmann, A.: Die Tuberkulose als Kinderkrankheit, München. med. Wchenschr., 1909, p. 388.

Aronade¹¹ gathered together the principal prevailing opinions about tuberculosis in infancy, speaks of observations of his own concerning the spread of the infection in tuberculous families, and mentions the absence of the cutaneous reaction in erysipelas. His opinion that the prognosis in tuberculosis in infancy, with the exception of that of the bones and joints, is absolutely bad, seems to Schelble to be pessimistic.

Beitzke¹² found in the autopsies of 397 children that the frequency of tuberculosis up to the fifteenth year was 27 per cent. (the new-born baby is not included in these figures), and of those 16 per cent. had fatal tuberculosis. Of these 10 per cent. were, during the first year of life, 41 per cent. from the first to the fifth year, and 65 per cent. from the sixth to the fifteenth year. In this latter group two-thirds had tuberculosis. The course of the disease is shown by the following figures: In the first year two-thirds died of tuberculosis, in the first to fifth, three-fourths; and from the sixth to fifteenth, one-tenth. The striking fact that fewer babies than children from 1 to 5 years died of tuberculosis may possibly be explained by the small number of tuberculous babies (11). Among the twenty cases of latent tuberculosis, the mesenteric glands were infected fourteen times and the bronchial glands five times. These figures are noteworthy.

Albrecht¹³ found in 3,213 autopsies of children that 33 per cent. were tuberculous, of which 18 per cent. were babies, 25 per cent. between the ages of 1 to 6 years and 17 per cent. between the ages of 6 to 12 years. The first year that it was necessary to report all cases of tuberculosis in Denmark was 1906. Saugmann²⁰ obtained interesting data from the statistics of this year: 4½ per cent. of the population of Denmark were reported as tuberculous. Of these 44.6 per cent. were males and 55.4 per cent. females. Only 0.9 per cent. of the entire population had tuberculosis under 10 years of age and 10.4 per cent. between 25 to 30 years. About 10 per cent. of the total deaths were due to tuberculosis.

According to Karlsson,¹⁹ who examined 15,219 school children in Stockholm, there were: Pulmonary consumption in 1.6 per cent.; suspicious signs of pulmonary tuberculosis 2.2 per cent.; enlarged glands (tuberculous?) 65.0 per cent.; presumably tuberculous glands, 10 to 30 per cent.; bone and joint tuberculosis 0.57 per cent.

Hamburger¹⁶ tested the tuberculin reaction of children who in all probability had not come in contact with tuberculosis, in order to establish the real frequency of tuberculosis in the children of Vienna. He found that the incidence in the different years of life, made a rapidly ascending curve which reached a high point of about 94 per cent. in the fourth period (eleventh to fourteenth years). Higher figures in the early years of life found by autopsy or the tuberculin reaction, may be explained by the segregation of the very sick tuberculous children in hospitals. Schlossmann²¹ believes that the incidence of 90 per cent. of tuberculosis in puberty as impossible. Hamburger's well known early work was done in a hospital clinic which was not representative. Only 50 to 56 per cent. of hospital children of Dusseldorf between 13 and 14 years reacted to tuberculin. Of 105 children of all ages in private practice only very few showed that they were infected with tuberculosis. He believes that the children of property owners are less easily infected. Schlossmann believes that Hamburger's figures will discourage us in the fight against tuberculosis. Hamburger¹⁷ defends himself against the contention that he drew too broad conclusions from a non-representative material, and says that his figures should not discourage us, since it is known that only a small number of these children have active tuberculosis in later life.

According to Franz¹⁴ 38 per cent. to 76 per cent. of the healthy soldiers between the ages of 21 and 23 years reacted to tuberculin. Only a small number of these individuals showed clinical manifestations of tuberculosis during the following years.

Hillenberg¹⁸ examined the school children of one city with the von Pirquet reaction and found that at puberty only 44 per cent. reacted, and furthermore, that only 8 per cent. reacted of those who had entered school recently, while 32 per cent. of those who had been in school one year reacted. He did not believe that the infection of these children had taken place in school. At all events the above figures are contrary to Hamburger's and are more like those found by Schlossmann in the Dusseldorf Hospital. Hamburger's opinion that "almost everyone acquires tuberculosis once during his life and usually during childhood," cannot, according to these findings, be of general application. Hillenberg examined only adults and found that the number of those with tuberculosis increased from the fifteenth to the thirty-ninth year.

Such observations modify the opinion of those authors very little who wish to stigmatize tuberculosis as a disease of childhood. Even with the data that at puberty 90 per cent. of the city dwellers react to tuberculin, one has no right to conclude that tuberculosis is a disease of childhood, since we know that a relatively small number of those who react to tuberculin at puberty and between 20 and 23 years become clinically tuberculous. Conversely one should find out how many of those at puberty who do not react to tuberculin become tuberculous in one year's time. One must consider seriously Hillenberg's opinion that slight infections of the glands may act as a means of bringing about a natural immunity against tuberculosis.

Fränkel¹³ reported in the first two numbers of the medical statistical news and emphasizes from the bulky statistics of the first part that in the provinces where the greatest efforts were made in fighting tuberculosis there was the largest decrease in the mortality. For example, in the province of Westphalia during the year 1907 there were 64 per cent. less deaths from tuberculosis than in the year of 1877. In the second part, which contained a summary of the mortality, with cause of death, and age at death in the cities, we see that during the year of 1908 for every 10,000 of population only sixteen died of tuberculosis, while in 1886, thirty-six died. Fränkel believes that in forty years' time tuberculosis has ceased to be a disease of importance.

Gottstein¹⁵ does not believe that the decrease of tuberculosis is the result of the increase of the sanatorium for diseases of the lungs and refers to Newsholm's statistics. This English writer believes that the segregation of open incurable tuberculosis in sanatoria is an important factor in preventing its spread.

B. HEREDITY AND PREDISPOSITION

22. Bergmann, A.: Ueber kongenitale Tuberkulose beim Rindvieh, Zentralbl. f. Bakteriolog., lii, 193.

23. Jungmann, P.: Beiträge zur Freundschens Lehre von Zusammenhang primärer Rippenknorpelanomalien mit Lungentuberkulose und Emphyse, Frankfurter Ztschr. f. Pathol., 1909.

24. Linden, K.: Untersuchungen über den Einfluss von Notjahren auf Tuberkulosehäufigkeit, sowie die Latenz der Tuberkulose auf Grundlage der Kassation, Wien. klin. Wchschr., 1909, p. 1448.

25. Lubliner, L.: Tuberkulose und Schwangerschaft, Lodz., 1909, Giwzlica No. 8.

26. Neumann, W., and Wittgenstein, H.: Das Verhalten der Tuberkelbazillen in den verschiedenen Organen nach intravenöser Injektion, Brauer's Beitr., 1909, xlii.

27. Weber, F. P., and Kirkness, W. R.: Eine Bemerkung über das Körpergewicht Lungentuberkulose, Ztschr. f. Tuberk., 1909, p. 224.

Family Predisposition.—Hillenberg¹⁸ studied carefully the general health of children with a positive von Pirquet and the health of the other members of families, and came to the conclusion that tuberculosis was present in only 15 per cent. of the families of the children with positive reactions. In the other 85 per cent. the source of infection was not in their own families. Of the 120 healthy families whose children reacted positively there were twenty-two families and their connections who did not react once to tuberculin. A careful study of

the homes and neighborhood showed that not one of the children could have been infected from tuberculous neighbors; the source of infection of one-half of the children was unknown. The food in the first year of life had no influence on the outbreak of tuberculous infection. No connection was found between milk from tuberculous animals and infection. His studies of the influence of heredity are interesting.

Jungmann²³ found in thirty-four autopsies lessened development of the first rib. Twenty of these had advanced phthisis; three times the tuberculosis was healed. He found normal cartilages in twenty-seven with tuberculosis of the lungs; in sixteen cases the tuberculosis was healed. He considers that his figures support Freund's teachings.

Neumann and Wittgenstein²⁶ found that the lungs had an especial predisposition for tuberculosis when tubercle bacilli were injected intravenously. Those bacilli which settled in the lungs preserved their virulence better than those which lodged in other organs.

Weber and Kirkness²⁷ found that in the material of the Mount Vernow Hospital (600 males and 100 females) tuberculosis had a predilection for those who were underweight.

Predisposition and Its Relation to Food.—Linden²⁴ believed that the increase of tuberculosis in the years of famine was a result of too little food.

C. CASUISTRY AND PATHOLOGIC ANATOMY

28. Aronade, O.: Ueber Säuglingstuberkulose, Brauer's Beitr., xiii.
29. Bartel, J.: Ueber Immunisierungsversuche gegen Tuberkulose, Wien. klin. Wehnschr., 1909, p. 117.
30. Cadbury, W.: Studies of Bone-Marrow in Pulmonary Tuberculosis, 5th An. Rep. H. Phipps Inst.
31. Chausse, M.: La tuberculose intestinale chez le boeuf, Ann. d. l'inst. Pasteur, 1909, p. 809.
32. Escherich, Th.: Was nennen wir Skrofulose? Wien. klin. Wehnschr., 1909, p. 224.
33. Everling, K.: Beitrag zur Lehre von der papillären Tuberkulose der Portio vaginalis, Berl. klin. Wehnschr., 1909, p. 1146.
34. Forkel, W.: Ein Fall von einseitiger, aufsteigender Tuberkulose im Urogenitalapparat, München. med. Wehnschr., 1909, p. 2003.
35. Heister, A., and Schall, H.: Ein Fall hochgradiger Bronchialdrüsentuberkulose ohne klinische Symptome, Brauer's Beitr., 1909, xiv.
36. Jönke: Untersuchungen zur Frage des Vorkommens latenter Tuberkelbazillen in den intermuskulären Lymphdrüsen generalisiert tuberkulöser Rinder, Virchow's Arch. f. path. Anat., 1909, p. 563.
37. Köhler, F.: Ueber die Beziehungen des Nervensystems zur Entstehung und Entwicklung der Lungentuberkulose, VIII intern. Tuberkulosekonferenz, 1909.
38. Kretz: Ueber ein junges Stadium der experimentellen hämatogenen Lungentuberkulose, Verhandl. d. Deutsch. path. Ges., 1909.
39. Landis: Fibrosis of the Lungs, 5th An. Rep. H. Phipps Inst., 1909.
40. Leiner and Spieler: Zur dissimulierten Hauttuberkulose im Kindersalter, Verhandl. d. Ges. f. Kinderh.
41. Levy, E.: Ueber die Erzeugung von tuberkulösen Lungenkavernen im Tierexperiment und deren Bedeutung, Zentralbl. f. Bakteriöl., lxi, 476.
42. Liebermeister, G.: Studien über Komplikationen der Lungentuberkulose und über Verbreitung der Tuberkelbazillen in den Organen und im Blut der Phthisiker, Virchow's Arch. f. path. Anat., 1909, p. 332.
43. Merkel, H.: Zur Kenntnis der primären Tuberkulose der Nasenrachenschleimhaut, München. med. Wehnschr., 1909, p. 1165.
44. Mohr, R.: Ueber einen Fall von Tuberkulose des Lendenmarkes, Verhandl. d. Deutsch. path. Ges., 1909, p. 337.
45. Moro: Lymphatismus und Skrofulose, München. Ges. f. Kinderh.
46. Moss, L.: The Relation of Bovine to Human Tuberculosis, Bull. Johns Hopkins Hosp., 1909, p. 39.
47. Raw, N.: Is Lupus Caused by the Bovine Tuberculosis? Tuberculosis, 1909, p. 295.
48. Reines, S.: Ueber die Beziehungen der Sklerodermie zur Tuberkulose, Wien. klin. Wehnschr., 1909, p. 1124.
49. Römer, P.: Ueber experimentelle kavernöse Lungentuberkulose, Berl. klin. Wehnschr., p. 813.
50. Römer, P.: Ueber Tuberkuloseimmunität, Ärztliche Verhandlungen, Marburg, May, 1909.
51. Römer, P.: Weitere Versuche über Immunität gegen Tuberkulose durch Tuberkulose, zugleich ein Beitrag zur Phthisiogenese, Brauer's Beitr., 1909, iii.
52. Schütz, A., and Vidéky, R.: Ueber den Zusammenhang der exsudativen (phlyktänulären) Augenerkrankungen und der Tuberkulose nebst Erfahrungen über den Wert der Kutanen und subkutanen Tuberkulindiagnostik, Wien. klin. Wehnschr., 1908, No. 37.
53. Sittler: Klinische Betrachtungen über Skrofulose, Würzburger Abhandl., 1909, p. 9.

54. Stieda, A.: Zur Symptomatologie der Tuberkulose des Ileosakralgelenkes, *Berl. klin. Wchnschr.*, 1909, p. 242.

55. Theodor: Ein Fall von tuberkulöser Nephritis nach einer Angina bei einem sonst gesunden Kind, *Arch. f. Kinderh.*, 1909, p. 363.

56. Winternitz, M.: Tuberculosis of the Parathyroid Gland and Its Relation to the Occurrence of Tetany in Tuberculous Meningitis, *Bull. Johns Hopkins Hosp.*, 1909, p. 269.

57. Zickgraf, G.: Ueber die Komplikation der Lungentuberkulose von seiten der oberen Luftwege, *Ztschr. f. Tuberk.*, 1909, p. 480.

Merkel⁴⁸ added to the four proven cases of primary tuberculosis of the nasal mucous membranes, another case in a woman aged 60. Forkel¹⁴ described a case of unilateral ascending tuberculosis of the genito-urinary apparatus, whose pathologic anatomy supported Baumgarten's teachings that tuberculosis cannot ascend so long as there is no obstruction to the urinary excretion. Theodor⁵⁵ reported the appearance of tuberculosis of the kidney after angina. Six months previous to the angina the urine had shown nothing abnormal, afterwards tubercle bacilli were found in the urinary sediment. Three years later the child died of tuberculous meningitis and tuberculosis of the kidney.

Cadbury⁸ found in his studies of the bone marrow in phthisis besides a very varied cellular composition of the marrow in the different bones, an increase in the lymphocytes in disease of the lymph-glands. Tubercle bacilli were found in 63 per cent. of the cases either by bacteriologic examination or by animal injection. Good reproductions of the microscopic picture accompany the text.

Raw⁴⁷ thought that lupus was caused by the bovine bacillus because treatment with human tuberculin did not help. Leiner and Spieler⁴⁰ were able to demonstrate isolated acid-fast bacilli in a follicular eruption. They speak of acute hemorrhagic miliary tuberculosis of the skin and of disseminated miliary lupus and the points of differential diagnosis of these three affections; they emphasize the fact that a sharp distinction cannot always be made.

Kretz³⁸ reports some experiments undertaken to determine whether small hemorrhages at the beginning of pulmonary tuberculosis were caused by infection at two separate times or whether they were brought about in each instance during the development of the infection and represent a stage of the change of reaction of the body. The experiments showed that such hemorrhages might come after a single subcutaneous infection and were the result of disease of the arteries at the beginning of phthisis.

Liebermeister⁴² found the tubercle bacillus in the blood of patients with phthisis several months before death. This distribution of the tubercle bacillus generally does not lead to miliary tuberculosis. He found histologic changes in almost all of the organs of those with phthisis, which either showed the picture of tuberculosis or appeared as foci of chronic inflammation. Tubercle bacilli were frequently found in these changes. These atypical processes were found most often in the veins at the nerve-roots, the kidney, heart, liver and skin.

Römer⁴⁹ was able to produce true consumption with cavity formation in animals with chronic tuberculosis and increased resistance by reinfecting them with large doses. He thought that the fact that cavity formation in the lungs and not miliary tuberculosis resulted, was evidence that cavities are evidence of immunity. Levy made the same observations.

Bartel²⁹ observed that the course of the disease was different in those animals which had been "treated beforehand." He also found that the virulence of the tubercle bacillus increased in the tissues of organs, especially in the lymphatic system, and he concluded, therefore, that the mode of entrance to the body was of especial significance in the question of immunity.

Römer⁵⁰ inoculated tuberculous and healthy guinea-pigs in the skin with equal amounts of tubercle bacilli and found that the healthy animals had a typical "impftuberculose" at a dilution of 1 g. to 10,000 and 100,000 physiologic salt solution, while in those animals with chronic tuberculosis (of 3-4 months duration) the skin only became diseased at a dilution of 1:1000 in a few of the animals.

Schütz and Vidéky⁵² divided phlyctenular diseases of the eye into those with a basis of exudative diathesis and those due to tuberculosis. They place those phlyctenulars which react to tuberculin in the second group. There are many which do not react to tuberculin in any form.

Sittler⁵³ classifies those symptoms as scrofulous which were formerly grouped under the name of exudative diathesis without tuberculosis. No author denies that if tuberculosis is superimposed on a diathesis, as the arthritic diathesis of the French, Czerny's exudative diathesis, or the so-called "lymphatismus," its outcome is less favorable and the boundaries between the diathesis without tuberculosis and the general picture known as scrofula, are not obliterated. The changes of the skin on the face of scrofulous children may be mentioned (one cannot say whether these children are already infected with tuberculosis); one finds most frequently on the skin of the cheeks a round apparently discrete patch with small scales. After a few days the flecks disappear and there is a diminished amount of pigment present. The whole thing lasts a few days. Escherich⁵⁴ and Moro⁴⁵ and many other pediatricians consider scrofula as a reaction of an exudative diathesis to infection with tubercle bacilli.

D. MODE OF INFECTION

58. Albrecht, H.: Ueber Tuberkulose des Kindesalters, Wien. klin. Wchnschr., 1909, p. 327.

59. Bartel, J.: Zur Frage der Infektionswege der Tuberkulose, Wien. klin. Wchnschr., 1909, p. 115.

60. Baumgarten: Welche Ansteckungsweise spielt bei der Tuberkulose des Menschen die wichtigste Rolle? Deutsch. med. Wchnschr., 1909, p. 1729.

61. Escherich, Th.: Die Infektionswege der Tuberkulose insbesondere im Säuglingsalter, Wien. klin. Wchnschr., 1909, p. 515.

62. Geipel and Schmorl: Diskussionsbemerkungen in der Gesellschaft für Natur und Heilkunde, Dresden, 20 Februar, 1909.

63. Hohlfeld: Ueber die Bedeutung der Rindertuberkulose für die Entstehung der Tuberkulose im Kindesalter, Verhandl. d. Ges. f. Kinderh.

64. Huguenin, B.: Nachweis von Tuberkelbazillen im Blut eines Fötus, Zentralbl. f. Bakteriöl., 1909, p. 394.

65. Rietschel: Ueber kongenitale Tuberkulose, Jahrb. f. Kinderh., 1909, lxx.

Baumgarten⁶⁰ believes that air-borne tuberculosis is possible and that the intestinal origin explains infection in the intestine by the bovine bacillus very well.

Albrecht⁵⁸ in a very large number of post-mortems of children (over 2,000) found only 0.66 per cent. of which were surely primary intestinal tuberculosis. In by far the majority of cases, he found the primary lesion in the lungs. It is interesting to note that he did not find a single case of tuberculosis of the cervical lymph-nodes without infection of the lungs or the tracheobronchial lymph-nodes. He found one isolated case of tuberculosis of the adenoid. He believes that there is also an affinity of the tubercle bacillus to glandular tissue in hematogenous tuberculosis. This is shown by the frequency of bone tuberculosis, which almost always begins in the bone marrow. He has never seen this type of tuberculosis without tuberculosis of the lungs or bronchial glands.

Hohlfeld⁶³ contrary to the statistics of Albrecht, finds that primary intestinal tuberculosis is relatively frequent in Leipsic and believes that raw milk products must be considered as sources of infection of bovine tuberculosis.

Escherich⁶¹ came to the conclusion, from his examination of clinical and anatomic material, and believes, that in aerogenous tuberculosis originating in the center of the lung with walling off and caseation of the bronchial lymph-glands and the terminal rupture of a caseous center into the blood-stream or a bronchus, we have the typical course of tuberculosis which is characteristic for infancy.

Bartel⁵⁹ speaks of the great difficulties in finding the mode of entrance of tuberculosis by autopsy and of passing judgment. Conclusions can only be based on examination of lymphoid tuberculosis.

Huguenin⁶⁴ was able to demonstrate by injecting guinea-pigs the presence of tubercle bacilli, in the heart-blood of a 6-months' fetus whose mother had tuberculosis. Neither the fetus nor the placenta were anatomically tuberculous.

Rietschel⁶⁶ communicated a case of unquestionable hereditary tuberculosis. Infection after birth was excluded. The baby died at 3 months of age with general tuberculosis. It is interesting that the von Pirquet was always negative. This was explained by the lack of resistance of young babies to tuberculosis. Rietschel assumed that the infection had taken place intrapartum from the placenta. Unfortunately this was not examined.

Geipel⁶⁷ thinks it improbable that a fetus can become infected with tuberculosis without the presence of tuberculosis of the placenta, but if there is tuberculosis of the placenta, infection of the fetus does not necessarily follow.

Schmorl⁶⁸ does not consider tuberculosis of the placenta rare, but does think fetal tuberculosis rare. He believes that the transmission of bacilli from the mother to the child by means of placental tuberculosis can only take place at the time of birth, when there are powerful contractions of the uterus which tear the tuberculous areas, and there is lessened resistance on the part of the placenta. Transmission of tuberculosis need not be feared earlier since the tuberculous changes act as a wall, which makes it difficult for the bacilli to get out of the placental tubercles. The rare case of infection *in utero* may be caused in different ways: by the blood-vessels, through the amniotic fluid; by the intestines; by the lungs. Tuberculosis of the fetus or infection at birth results very quickly in death, and it is very improbable that it lies latent until a later age.

Bergmann⁶⁹ found during four years 108 cases of congenital tuberculosis in horned cattle; four times in the fetus and 104 times in calves, the oldest of which was three days old.

E. BACTERIOLOGY AND SERUM

66. Bauer, J.: Ueber Immunitätsvorgänge bei der Tuberkulose. Brauer's Beitr., 1909, xlii.

67. Bauer, J.: Die passive Uebertragung der Tuberkulosenüberempfindlichkeit. München. med. Wchnschr., 1909, p. 1218.

68. Bauer, J.: Ueber den Nachweis der Antigene bei der Komplementablenkung der Tuberkulose. München. med. Wchnschr., 1909, p. 71.

69. Bohme, A.: Ueber Tuberkulose-Immunoopsonine. München. med. Wchnschr., 1909, p. 1184.

70. Deycke, P., and Much, H.: Bakteriolyse und Tuberkelbazillen. München. med. Wchnschr., 1909, p. 1985.

71. Eber: Weitere experimentelle Beweise für die nahe Verwandtschaft der beim Menschen und beim Rinde vorkommenden Tuberkelbazillen und die Möglichkeit einer Umwandlung menschlicher Tuberkelbazillen in rindervirulente Formen. München. med. Wchnschr., 1909, p. 2215.

72. Eitner, E., and Störk, E.: Serologische Untersuchungen bei Tuberkulose der Lunge und der Haut. Zentralbl. f. Bakteriöl., 1909.

73. Ellermann, V., and Erlandsen: Ueber Sensibilisierung bei der kutanen Tuberkulinreaktion. Brauer's Beitr., xiv.

74. Engel: Ueber das Verhalten der kindlichen Tuberkulose gegen Tuberkulin. Brauer's Beitr., 1909, xlii.

75. McFarland, J., and Beardsley, G.: Elimination of Tubercle Bacilli by the Intestines. 5th An. Rep. H. Phipps Inst., 1909.

76. Fontes, A.: Untersuchungen über die chemische Natur der den Tuberkelbazillen eignen Fett- und Wachstumsarten und über das Phänomen der Säureresistenz. Zentralbl. f. Bakteriöl., 1909, xlix, 317.

77. Fontes, A.: Ueber eine in den tuberkulösen Lymphdrüsen vorhandene, Tuberkelbazillen tödende Substanz. Zentralbl. f. Bakteriöl., 1909, l, 78.

78. Fornet, W., and Porter, A.: Opsonine und Antiopsonine in ihrer Wirkung auf Tuberkelbazillen. Zentralbl. f. Bakteriöl., 1909, li, 138.

79. Frugoni, C.: Studien über das Blutserum der Tuberkulösen und die Exsudate der serösen Höhlen mittels Komplementbindung. Berl. klin. Wchnschr., 1909, p. 1724.

80. Fua, R., and Koch, H.: Zur Kenntnis der mit Tuberkulin komplementbindenden Stoffe im Serum tuberkulöser Kinder. Brauer's Beitr., 1909, xiv.

81. Grüner, O.: Ueber die Herabsetzung der Tuberkulinempfindlichkeit Tuberkulöser während der Masern. München. med. Wchnschr., 1909, p. 1681.

82. Grüner, O.: Ueber Agglutination bei tuberkulösen Kindern. Brauer's Beitr., 1909, xiv.

83. Koch, H.: Beiträge zur Frage der Komplementbindungsreaktion bei Tuberkulose. München. med. Wchnschr., 1909, p. 2310.

84. Laub, M., and Novotny, J.: Ueber komplementbindende Substanzen bei Tuberkulose. Wien. klin. Wchnschr., 1909, p. 1104.

85. Liebermeister, G.: Ueber die nach Ziehl nicht darstellbare Form der Tuberkelbazillen. Deutsch. med. Wchnschr., 1909, p. 1224.

86. Lippmann, A.: Zum Nachweis der Tuberkelbazillen im strömenden Blut der Phthisiker. München. med. Wchnschr., 1909, p. 2214.

87. Pfeiffer, H., and Persch, R.: Untersuchungen über die Einwirkung von Verdauungsfermenten auf Tuberkulin. Wien. klin. Wchnschr., 1909, p. 1149.

88. Pickert, M.: Ueber natürliche Tuberkulinresistenz, Deutsch. med. Wchnschr., 1909, p. 1013.

89. Pickert, M.: Ueber das Gesetzmässige Auftreten von Tuberkulinantikörpern im Laufe der spezifischen Behandlung und seine Bedeutung für die Therapie, Deutsch. med. Wchnschr., 1909, p. 1514.

90. Rabinowitsch, M.: Eine neue Methode zur genauen Bestimmung der Quantität der Tuberkelbazillen bei Impfversuchen, Deutsch. med. Wchnschr., 1909, p. 1102.

91. Schmitz, E.: Experimentelle Untersuchungen über die Virulenz latenter tuberkulöser Herde bei Menschen, Rind und Schwein, Frankf. Ztschr. f. Pathol., 1909, p. 88.

92. Siebert, C.: Zur Biologie der Tuberkelbazillen, Zentralbl. f. Bakteriöl., li, 305.

93. Von Szabóky, J.: Präzipitationsuntersuchungen bei Tuberkulösen, Ztschr. f. Tuberk., 1909.

94. Wehrli, E., and Knoll, W.: Ueber die nach Much färbbare granuläre Form des Tuberkulosevirus, Brauer's Beitr., 1909, p. 14.

Virulence.—Schmitz⁹¹ found virulent tubercle bacilli in totally calcified tubercles in man, cattle and pigs.

Fontes⁷⁵ believes that there is a substance in the lymph-glands of guinea-pigs which has the power of reducing the number of tubercle bacilli *in vitro*.

Much and Deycke⁷⁰ obtained bacteriolysis of the tubercle bacillus *in vitro* with lecithin in a few minutes, also with cholin and neurin. The bovine type was not acted on so easily as the human type.

McFarland and Beardsley⁷⁵ did not find tubercle bacilli in the feces of guinea-pigs and rabbits after intravenous injections of tubercle bacilli and only found them occasionally in general tuberculosis.

Serum.—Pickert⁸⁸ was able to show by means of a special method devised by Löwenstein and himself (see Schelble's Ref., 1908) that the serum of patients with pulmonary tuberculosis who had had specific treatment occasionally had the action of neutralizing the action of tuberculin on the skin of tuberculous subjects. He found this property present more often in the serum of those patients in whom the disease was running a favorable course. These patients reacted weakly to diluted tuberculin and only reacted to 5 per cent. or stronger. After the injection of large doses of tuberculin, he noticed an increased power of neutralization in the serum and recommends, therefore, tuberculin therapy.

Bauer⁶⁸ tried whether Marmorek's serum mixed with the serum of a tuberculous man, gave fixation of the complement. The reaction was negative with ten tuberculous children as well as with pure "tuberkelbazillen-derivaten." He said furthermore, that the antigen groups for tuberculin and the emulsions of bacilli have characteristics of their own and said that the use of the antigen is valueless for diagnostic purposes.

Fua and Koch⁸⁰ were not able to show complement fixation in either the serum or the spinal fluid of untreated children, who had tuberculosis, and found it only in one-third of those treated.

Laub and Novotny⁸⁴ found the fixation of the complement positive now and then in tuberculous patients post-mortem but they also found it in non-tuberculous patients. They, therefore, consider that the reaction is not specific.

Koch⁸³ found antibodies only in children who had had specific treatment.

V. Szabóky⁹³ found a precipitin between the blood-serum of tuberculous patients and rabbits which had been injected with the protein part of tuberculous tissue. He could not show any connection between the precipitating power of the blood-serum of tuberculous patients and the stage of the disease. The fact that many tuberculous sera precipitate physiologic salt solutions, lipid-free extracts of tubercle bacilli, and lecithin makes the specific test of precipitins less valuable.

Frugoni⁷⁹ gives the conclusions of his studies on fixation of the complement, without the protocol. He does not get constant results in determining the etiology of exudates by fixation of the complement.

According to Grüner⁸² the phenomena of agglutination has theoretical interest, but is of no practical value.

Bauer⁶⁷ tried to give passive immunity to normal guinea-pigs by injecting them with the blood-serum of tuberculous guinea-pigs and man. The reaction with fever was most definite when the tuberculin was injected twenty-four to forty-eight hours after the preparatory treatment. It was to be seen for several days. The guinea-pigs which were made anaphylactic did not become tuberculous.

Fornet and Porter⁷⁵ found "thermolabile" opsonins in the serum of tuberculous and healthy patients. They found that the antiopsonins in the heated or dialyzed serum attached themselves only to the thermolabile opsonins of fresh serum and they believe that possibly the variation of the opsonic index in an infected organism can be explained by the formation of antiopsonins.

Böhme⁹⁰ did not find any "tuberkulosebakteriotropinen" in the blood of normal men; he found a small amount in those with mild tuberculosis and none in miliary tuberculosis. Treatment with new tuberculin increased these bodies. He found no definite connection between the course of the disease and the amount of "bakteriotropin" and therefore considers them of no prognostic value. Serum rich in "bakteriotropin" can be made more powerful by heating. The variations in the opsonic curve can only be explained in part by the "bakteriotropin." There must be other factors which play a part.

Grüner⁸¹ tested the puncture reaction "tuberculinstichreaction" in thirteen tuberculous individuals with measles and found that the sensibility to tuberculin was greatly diminished during the exanthema and that it increased rapidly about eight days after the rash broke out. He believes that the diminution of the reaction in measles is not due to an antituberculin in the serum of those with measles but to the sensibility of the patient with measles against the tubercle bacillus.

F. DIAGNOSIS

95. Ahmann: Ueber eine neue Kontrastfärbung zur Darstellung intrazellulärer Tuberkelbazillen im Auswurf. München. med. Wehnschr., 1909, p. 658.

96. Bornbach, P.: Vergleichende Untersuchungen über den Wert der Bordetschen und Pirquetschen Reaktion. Ztschr. f. Tuberk., p. 491.

97. Bernhardt, G.: Ueber die Verwendung von Antiformin und Irgoin für den Nachweis der Tuberkelbazillen im Sputum. Deutsch. med. Wehnschr., 1909, p. 1428.

98. Berha, F.: Ueber das Verhältnis der zur Darstellung gelangten Tuberkelbazillen bei Sputumfärbemethode. Zentralbl. f. Bakteriöl., II, 678.

99. Von Betegh, L.: Ueber eine neue Methode zur Darstellung der Tuberkelbazillensporen. Zentralbl. f. Bakteriöl., 1909, xlix, 461.

100. Buschke, A., and Kuttner, P.: Zur Technik der v. Pirquetschen Reaktion, Berl. klin. Wehnschr., 1909, p. 1304.

101. Caan, A.: Vergleichende Untersuchungen über neuere Methoden der Tuberkul-pilzfärbung. Zentralbl. f. Bakteriöl., 1909, xlix, 637.

102. Cohn, M.: Zur Anatomie, Pathologie und Röntgenologie der Lungentuberkulose, Berl. klin. Wehnschr., 1909, p. 1304.

103. Dembinski, B.: Ueber die klinische Bedeutung der Calmetteschen Reaktion, Ztschr. f. Tuberk., 1909, p. 297.

104. Blackwood, Douglas J.: The Opsonic Index in Pulmonary Tuberculosis, 5th An. Rep. H. Phipps Inst., 1909.

105. Ellermann, V., and Erlandsen, A.: Ueber quantitative Ausführung der kutanen Tuberkulinreaktion und über die klinische Bedeutung des Tuberkuliniters, Deutsch. med. Wehnschr., 1909, p. 436.

106. Franz, K.: Ergebnisse mehrjähriger Beobachtungen an 1,000 im Jahre 1901 bis 1902 mit Tuberkulin zum diagnostischen Zwecke injizierten Soldaten, Wien. klin. Wehnschr., 1909, p. 991.

107. Gasis, D.: Ueber eine neue Reaktion der Tuberkelbazillen und eine darauf begründete differenzialdiagnostische Färbungsmethode derselben, Zentralbl. f. Bakteriöl., xl, 111.

108. Gabrilowitsch, J.: Zur Sputumuntersuchung bei Phthisikern, Ztschr. f. Tuberk., 1909.

109. Hamburger, F.: Ueber die Stichreaktion bei der Diagnose kindlicher Tuberkulose, München. med. Wehnschr., 1909, p. 22.

110. Hatano: Ueber kombinierte Färbungsmethoden für Tuberkelbazillen, Berl. klin. Wehnschr., 1909, p. 628.

111. Hellesen, E.: Ueber die kutane Tuberkulinreaktion im Kindesalter, Jahrb. f. Kinderh., 1909, p. 663.

112. Kaminer, S.: Hat die Ophthalmoreaktion für die Prognosenstellung bei der Tuberkulose der Schwangeren Bedeutung? Berl. klin. Wehnschr., 1909, p. 392.

113. Kögel, H.: Ueber den Nachweis von Tuberkelbazillen im Sputum nach der Doppelmethode von Ellermann-Erlandsen, Deutsch. med. Wehnschr., 1909, p. 2105.

114. Krämer, C.: Bronchialdrüsendämpfung im Interskapularraum und ihre Bedeutung für die Diagnose und spezifische Therapie der Tuberkulose, Brauer's Beitr., 1909, xiv.

115. Krause, P.: Ueber den derzeitigen Stand der Röntgen-Diagnostik der Lungentuberkulose, Tuberkulosis, 1909, viii, 1.

116. Kritz, G.: Die Pirquetsche Reaktion bei Säuglingen, Med. Klin., 1909, p. 175.

117. Kutby, O.: Das Akromialsymptom bei Lungentuberkulose, Ztschr. f. Tuberk., 1909, p. 182.

118. Lange, L., and Nitsche, P.: Eine neue Methode des Tuberkelbazillennachweises, Deutsch. med. Wehnschr., 1909, p. 435.

119. Lier, W.: Ein Beitrag zum Nachweis des Tuberkelbazillus im Gewebe, Zentralbl. f. Bakteriöl., 1909, II, 678.

120. Mallinkrodt: Zur Klinik der Säuglingstuberkulose, Vereinigung niederhein-westfäl. Kinderärzte.

121. Meyer, K.: Zum Nachweis von Tuberkelbazillen im Sputum mittels Antiformin, *Tuberkulosis*, 1909, p. 71.
122. Naegeli-Akerblom, H., and Vernier, P.: Zur Diagnose und Therapie der Tuberkulose der Harnwege, 1909.
123. Ohm, W.: Kutanreaktion mit Eisentuberkulin, *Med. Klin.*, 1909, p. 504.
124. Poten and Griemert: Bei Pirquetsche Tuberkulinprobe bei Neugeborenen und ihren Müttern, *Deutsch. med. Wchnschr.*, 1909, p. 973.
125. Raw, N.: Specific Therapy in the Diagnosis and Treatment of Tuberculosis, IX Tuberkulosenkonferenz.
126. Rieder, H.: Die frühzeitige Erkennung der Lungentuberkulose mit Hilfe der Röntgen-Strahlen, *Deutsch. Arch. f. klin. Med.*, 1909, xcv, 62.
127. Roepke, O.: Ueber die heutige diagnostische und therapeutische Anwendung des Tuberkulins in der Praxis, *Med. klin. Wchnschr.*, 1909, p. 500.
128. Russow, K.: Ueber eine neue Kontrastfärbung zur Darstellung intrazellulärer Tuberkelbazillen im Auswurf, *München. med. Wchnschr.*, 1909, p. 920.
129. Sato, T.: Zur Diagnostik der Tuberkulose durch innerliches Einnehmen von Tuberkulin, *Brauer's Beitr.*, 1909, xiv.
130. Schaefer: Das Vorkommen und die Bedeutung halbseitiger erhöhter Temperaturen bei Lung-affektion, *Ztschr. f. Tuberk.*, 1909, p. 228.
131. Von Schaeven, E.: Nachweis spärlicher Tuberkelbazillen im Sputum, *Deutsch. med. Wchnschr.*, 1909, p. 1617.
132. Schick: Expiratorisches Keuchen als Symptom der Lungendrusentuberkulose im ersten Lebensjahr, *Verhandl. d. Gesellsch. f. Kinderh.*, 1909.
133. Schnitter: Nachweis und Bedeutung der Tuberkelbazillen im strömenden Phthisikerblut, *Deutsch. med. Wchnschr.*, 1909, p. 1566.
134. Schuster, H.: Die Prognose der klinischen Lungentuberkulose auf Grund der Wolff-Eimerschen Konjunktivalreaktion, *Ztschr. f. Tuberk.*, 1909.
135. Seeman, O.: Die Brauchbarkeit des Antiformins zum Nachweis von Tuberkelbazillen, *Berl. klin. Wchnschr.*, 1911, p. 628.
136. Sluka: Röntgen-Befunde bei Lungen- und Drusentuberkulose, *Verhandl. d. Gesellsch. f. Kinderh.*, 1909.
137. Von Sokolowski, D.: Diagnose und Therapie der beginnenden Lungentuberkulose mit Hilfe moderner diagnostischer und therapeutischer Methoden, *Berl. klin. Wchnschr.*, 1909, pp. 1880, 1936.
138. Von Szabóky, J.: Erfahrungen über die praktische Verwertung der Komplementbindung und anderer bakteriologischer und serologischer Untersuchungen bei der Diagnose der Lungentuberkulose, *Ztschr. f. Tuberk.*, 1909, 249.
139. Von Szabóky, J.: Agglutinationsversuche bei Tuberkulose, *Ztschr. f. Tuberk.*, 1909, p. 276.
140. Tedeschi, V.: Ueber Tuberkulinreaktion, speziell über eine Aurikulareaktion, *Arch. f. Kinderh.*, 1909, p. 189.
141. Turban: Anwendung spezifischer Mittel in der Tuberkulosedagnostik und Therapie, VIII intern. Tuberkulosenkonferenz.
142. Veit, E.: Ueber die Ergebnisse der Kutanreaktion nach v. Pirquet, *Mitt. a. d. Hamburger Staatskrankenanst.*, 1909, x, Part 11.
143. Vogt, E.: Einige Beobachtungen mit der Färbungsmethode der Tuberkelbazillen nach Demetrius Gasis, *München. med. Wchnschr.*, 1909, p. 1849.
144. Wehrauch, K.: Beiträge zur Färbung der Tuberkelbazillen und Granula im Sputum.
145. eWiss: Zur Morphologie des Tuberkulosevirus unter besonderer Berücksichtigung einer Doppelfärbung, *Berl. klin. Wchnschr.*, 1909, p. 1797.
146. Wolff-Eisner, A.: Die Prognosestellung bei der Tuberkulose mit besonderer Berücksichtigung der Balneologie nebst Bemerkungen über die Frühdiagnose und Tuberkulintherapie, *Berl. klin. Wchnschr.*, 1909, p. 890.
147. Wolff-Eisner, A.: Ueber Tuberkulinvaseline zur Anstellung der Konjunktivalreaktion, *München. med. Wchnschr.*, 1911, p. 226.
148. Wolff-Eisner, A.: Ueber Herdreaktionen und über die Verwendungsmöglichkeit der Konjunktivalreaktion in der Ophthalmologie, *Med. Klin.*, 1909, p. 1933.
149. Welff, P.: Ueber latentes Vorkommen der Munnschen Form des Tuberkelbazillus, *München. med. Wchnschr.*, 1909, p. 2312.

Tuberculin Diagnosis—Cutaneous, Intracutaneous, and Subcutaneous Methods:

Poten and Griemert¹²⁴ found negative reactions in thirty-five infants between one and fourteen days old and in four babies between three and four weeks.

Hellesen¹²¹ and Mallinkrodt¹²⁰ believe the cutaneous tuberculin reaction to be of clinical value.

Ellermann and Erlandsen¹⁰⁵ find that the sensibility against tuberculin of those with clinical tuberculosis six times as great as those without tuberculosis and believe that tuberculin dilutions are of value in determining the reaction of the body against the disease. An accurate standardization of the tuberculin used is necessary for such work.

Buschke and Kuttner¹⁰⁰ inject 25 per cent. A. T. into a cantharides blister and find the tuberculin reaction more sensitive than the von Pirquet; they do not attribute any practical significance to this modification.

Tedeschi¹⁴⁰ describes the superiority of the eye reaction. Ohm¹²³ recommends the cutaneous reaction with iron tuberculin (Dittborn and Scholz: *Deutsch. med. Wchnschr.*, 1908, No. 38) because a positive reaction means an active tuberculosis

especially in the adult, and the negative reaction rules out tuberculosis. These conclusions seem to the writer too optimistic in view of the fact that 28 per cent. of positive tuberculous patients have negative reactions and a relatively large number of those not sick with tuberculosis and the suspicious ones react positively. The method seems of value in children free from tuberculosis.

Veit¹⁴² considers the cutaneous reaction to be of equal importance in diagnosis in children to the subcutaneous injection of tuberculin.

Kritz¹¹⁶ saw a negative von Pirquet reaction five days ante-mortem in one case of pneumococcus meningitis which showed at autopsy tuberculosis of the bronchial glands and also fourteen days before death in a tuberculous child, and questions whether cachexia can change the power of reacting.

Hamburger¹⁰⁰ found that a negative cutaneous reaction is seldom absent in active tuberculosis but comes now and then. Schelble thinks that only two of the eight cases reported as active tuberculosis can be considered such; those are Cases 6 and 8. In Case 6 the absence of the reaction can be attributed to the cachexia.

Raw¹²⁵ is not convinced of the reliability of the Detre test with human and bovine tuberculin for the purpose of determining the kind of infection. Schütz and Videky⁶² believe from their experience that differentiating inoculation is useless on account of the great difference in the morphology of the papule and the time and course of the reaction.

Turban¹⁴¹ recommends subcutaneous injection and careful physical examinations as a reliable diagnostic method of finding pulmonary tuberculosis in the adult.

Roepke¹²⁷ believes that an elevation of the temperature contra-indicates subcutaneous injections of tuberculin.

Sahli¹⁰ completely rejects the diagnostic value of injections of tuberculin.

Eye Reaction.—Wolff-Eisner¹⁴⁷ recommends a 1 to 2 per cent. tuberculin vaselin ointment in the conjunctival reaction and discusses in conclusion the practical application of the reaction with *pros* and *cons* and emphasizes¹⁴⁸ again that a positive reaction means the presence of active tuberculosis, and accordingly is of great prognostic value. The conjunctival reaction is of little value in ophthalmology. It depends on the reaction of the inner eye and very small amounts must be instilled to be free from danger.

Schuster¹³⁴ considers the conjunctival reaction accidental. He believes that a prognosis can only be made from accurate examination of the lungs.

Dembinski¹⁰³ found a positive conjunctival reaction in 90 per cent. of those tuberculous, 55 per cent. of the suspicious cases, and 20 per cent. of the clinically non-tubercular. Turban¹⁴¹ considers the eye reaction dangerous, likewise Sahli¹⁰ and v. Szabóky¹³⁸ discuss the limitation of Calmette's procedure with cobra-poison, the agglutinations, and the opsonins. They conclude that bacteriologic examination is indispensable.

Serum.—The technic of estimating the opsonic index, according to Douglas Blackwood⁸ is too difficult for practical use in a clinic.

Fornet and Porter⁷⁸ find an opsonic index which goes from one extreme to the other in patients with advancing tuberculosis and consider this of reliable diagnostic importance. The action of the opsonins in inactive tuberculosis is not mentioned.

Turban¹⁴¹ discusses the conditions in which the opsonic index may be used in the diagnosis of active pulmonary tuberculosis.

Ahmann⁸⁵ describes a method of staining by contrast the protoplasm of the leukocytes and the tubercle bacilli, so that they may more easily be differentiated.

Russow¹²⁸ speaks of technic.

Diagnosis by Bacteriologic Examination.—Weihrauch¹⁴⁸ believes the Ziel stain valuable after previously treating the sputum with antiformin. Lange and Nitsche¹¹⁸ described a method of demonstrating the tubercle bacillus by KOH and ligroin. Schaeven¹²¹ is pleased with this method. Bernhardt⁹⁷ combined this

method with that of Uhlenhuth and Xylander. Kögel¹¹³ used the method of Ellermann-Erlandsen (*Ztschr. f. Hyg.*, 1908). Von Getegh⁹⁹ described a method of showing the spores of the tubercle bacillus with silver nitrate solution. Gasis used a new color method which depended on the combination of alkalies with the tubercle bacillus. Vogt,¹⁴³ MMV, thinks this method useful in staining bacilli, especially in differentiating them from the Smegma bacillus. Wolff¹⁴⁹ comes to the conclusion that Much's method gives useful results in demonstrating the tubercle bacillus, where the Ziel stain does not stain. Latent tuberculosis in lymph-glands can be shown with the Much stain. Liebermeister⁸⁵ showed that not only the tubercle bacillus but also many other bacteria contain granules and that therefore the granules of the tubercle bacillus can be confused with those of other bacteria; Gram-positive rods and rods with granules are only of diagnostic significance when other bacteria can be excluded. Wehrli and Knoll⁹⁴ say that when Much's method is used correctly it is very valuable. Lipmann⁸⁰ devised a method of bacterioscopic demonstration of the tubercle bacillus in the blood by dissolving blood with acetic acid and further treatment with antiformin. Schnitter¹³³ used Stauble's method of finding the tubercle bacillus in blood and thinks it is a valuable aid in difficult cases of differential diagnosis between typhoid fever, sepsis and miliary tuberculosis. Gabrilowitsch¹⁰⁸ proposed to simplify Gaffky's table because many numbers of this table have no significance in prognosis.

Physical and Roentgen-ray Diagnosis:

Schick¹³² discussed the symptom of expiration cough in tuberculosis of the lymph-nodes at the hilums of the lungs and considers it of value in diagnosis. Sluka¹⁵⁶ reports in detail the Roentgen findings in these cases and considers the diagnosis of tuberculosis of the bronchial glands in children during the first years of life certain when the following three symptoms are present: Expiratory cough, positive Pirquet reaction and characteristic Roentgen pictures of diseased glands in the lungs.

Some of the authors who discussed the paper, consider an inspiratory cough rare, and others considered the Roentgen diagnosis of bronchial glands of little value in early infection of the glands. Knöpfelmacher drew attention to the great value of temperature charts in such children.

Krause¹¹⁵ gave a historical sketch, described the technic, and communicates the results of Roentgen-ray examinations.

Schaefer¹⁵⁰ believes the differences of temperature in the axillæ is a failure to measure correct temperatures and that they are of no diagnostic value in localizing the tuberculosis in the lung.

G. PROPHYLAXIS

150. D'Almeida, J.: La tuberculose dans les écoles, VIII intern. Tuberkulosenkonferenz, 1909.

151. Altschul, Th.: Tuberkulose und Schule, VIII intern. Tuberkulosenkonferenz, 1909.

152. Bielefeldt, A.: Welche Massnahmen, sind zur Isolierung tuberkulöser Personen zu empfehlen? Brauer's Beitr., 1909, xiii.

153. Buhre, B.: Fürsorge in tuberkulösen Familien, insbesondere für die gesunden Kinder, VIII intern. Tuberkulosekonferenz, 1909.

154. Czerny, A.: Zur Prophylaxe der Tuberkulose, Berl. klin. Wehnschr., 1909, p. 2045.

155. Freund, R.: Fürsorge in tuberkulösen Familien, insbesondere für die gesunden Kinder, VIII intern. Tuberkulosenkonferenz, 1909.

156. Hart, C.: Zur Prophylaxe der Lungentuberkulose, *Ztschr. f. Tuberk.*, 1909, p. 201.

157. Helm, F.: Die Tätigkeit der internationalen Vereinigung gegen Tuberkulose, *Tuberkulosis*, 1909, p. 50.

158. Henschen, S.: On the Relation Between Alcoholism and Tuberculosis, *Tuberculosis*, 1909, p. 425.

159. de Jong, A.: Pasteurizing der Milch in Ruhe und Abötung von Tuberkelbazillen, *Zentralbl. f. Bakteriöl.*, 1909, p. 670.

160. Klehmet, F.: Das Tuberkulose-Wandermuseum des deutschen Zentralkomitees zur Bekämpfung der Tuberkulose, *Ztschr. f. Tuberk.*, 1909, p. 384.

161. Koch, F.: Ueber die Genese und Prophylaxe der mechanischen Disposition der Lungenspitzen zur Erkrankung an tuberkulöser Phthise, Brauer's Beitr., 1909, xiii.

162. Köhler, F.: Wohnungsreform und Tuberkulosebekämpfung, *Ztschr. f. Tuberk.*, 1909, p. 357.

163. Knopf, S. A.: The Popular Lecture in the Crusade Against Tuberculosis, *Tuberculosis*, 1909, p. 27.

164. Knopf, S. A.: Die moderne Tuberkulosebekämpfung vom sozialmedizinischen Standpunkt betrachtet, *Tuberkulosis*, 1909, p. 201.
165. Von Martínez, G.: Zur Frage einer Tuberkuloseversicherung, *Tuberkulosis*, 1909, p. 179.
166. Neander: Kinderfürsorge auf dem Lande, VIII intern. Tuberkulosekonferenz, 1909.
167. Neubecker: Welche gesetzlichen Bestimmungen stehen den öffentlichen Verbänden und Gemeinden im Kampf gegen die Tuberkulose zur Seite? *Tuberkulosis*, 1909, p. 119.
168. Résolutions du 4th Congrès medical latino américain, *Tuberkulosis*, 1909, p. 491.
169. Ritter and Vehling: Kindheitstuberkulose und Immunität, *Berl. klin. Wchschr.*, 1909, p. 1924.
170. Roepke and Busch, D.: Disinfektion der Wäsche Tuberkulöser, *Ztschr. f. Tuberk.*, 1909, p. 189.
171. Roepke: Ueber die Wohnungsdesinfektion bei Tuberkulösen, *Ztschr. f. Tuberk.*, 1909, p. 372.
172. Schmey, F.: Ueber die Beziehungen der Skrofulose und Tuberkulose, *Tuberkulosis*, 1909, p. 469.
173. Sell, F.: Belehrungskurse in Volkshelstätten, *Ztschr. f. Tuberk.*, 1909, p. 201.
174. Smit, H.: Ueber das Vorkommen von Tuberkelbazillen in der Milch und den Lymphdrüsen des Rindes, *Zentralbl. f. Bakteriöl.*, 1909, xlix, 33.
175. Sundell, C.: Einige Worte über die Wirksamkeit der Fürsorgestellen in Stockholm aus sozialem Gesichtspunkt, VIII intern. Tuberkulosekonferenz, 1909.
176. Swecney, F.: The Fight for the Child, *Tuberkulosis*, 1909, p. 538.
177. Von Unterberger, S.: Vererbung der Schwindsucht auf Grund von Riffel-Schlüterschen Ahnentafeln, VIII intern. Tuberkulosekonferenz, 1909.
178. Windstrand, A.: Der schwedische Nationalverein gegen die Tuberkulose, *Tuberkulosis*, 1909, p. 275.
179. Wiese, C.: Care of Tuberculous Families, VIII intern. Tuberkulosekonferenz, 1909.

According to Jong¹⁵⁹ not only the tubercle bacilli of cows' milk can stand pasteurization of 71 to 72 C. for a half an hour, but also those in the horse, goat, sheep, pig, cat and human milk. Such milk cannot be considered free from infectious agents. This report is of significance because Smit demonstrated tubercle bacilli in the milk of cows free from tuberculosis of the udder.

Henschen¹⁶⁸ drew attention to the fact that inebriety should be stopped; alcoholism is the principal cause of poverty and poverty is the fundamental cause of tuberculosis.

Köhler¹⁶² describes the influence of bad living on the spread of tuberculosis and proposes reforms in the hygiene. He reports the result of quiet moderate living of one thousand Rhenish workmen who had pulmonary tuberculosis; the effect on the children of the married ones was of especial interest.

Hart¹⁵⁸ does not consider that infection in childhood is synonymous with early or late tuberculosis. He recommended systematic exercises to develop the chest.

Ritter and Vehling¹⁶⁹ took very accurate histories in 206 cases of adult pulmonary tuberculosis and came to the conclusion that in 82 per cent. the infection was probably during childhood. The preponderance of severe diseases in those persons who have presumably not had tuberculosis in childhood is striking, as is the mild course of the diseases in those who have probably had tuberculosis.

A. Czerny⁶⁴ says that the children of individuals with tuberculosis, living in the same environs as their parents, are repeatedly infected, although possibly not tuberculous at first. He says that not only the nurse but also all persons who have the care of a young child should be examined for tuberculosis.

Neubecker¹⁶⁷ says that in Germany it depends on the will of the sick persons whether they will be treated or not.

Knopf¹⁶⁴ spread "rules" for preventing the infection of children with tuberculosis. These rules are short and easy to understand. The necessity of great care of the children in tuberculous families was brought up in the VIII International Conference on Tuberculosis and in the fourth *Congrès medical latino-américain*. When we hear from the different authorities how difficult it is to protect the healthy children from their phthisical elders, we come to the conclusion that "remorseless separation of the phthisical from their families is necessary."

Unterberger¹⁷⁷ is not hopeful of such "inhumane" treatment because the inherited predisposition and not the infection itself is principal cause. He recommends therefore that the energies be concentrated on strengthening the child.

H. THERAPY

180. Aronade: Ueber Säuglingstuberkulose, Verein Niederrheinisch-Westfälischer und Sudwestdeutscher Kinderärzte.
181. Baradat: L'Engadine en France, Tuberkulosis, 1909, p. 89.
182. Bartel, J., and Harth, R.: Ueber Immunisierungsversuche gegen Perlsucht, Zentralbl. f. Bakteriologie, 1909, p. 667.
183. Bartel, J., and Neumann, W.: Ueber Immunisierungsversuche gegen Tuberkulose, Zentralbl. f. Bakteriologie, 1909, p. 657.
184. Brauer and Engel: Die Tuberkuloseimmunität und spezielle Therapie, Brauer's Beitr., 1909, p. 13.
185. Bertarelli, E.: Ueber die Immunisierung des gesunden Menschen mit Kochschem Tuberkulin, Zentralbl. f. Bakteriologie, 1909, p. 353.
186. Brauer, L., and Spengler, L.: Erfahrungen und Ueberlegungen zur Lungenkollapstherapie, Brauer's Beitr., 1909, xiv.
187. Eber, A.: Weitere Beobachtungen über Anwendung des v. Behringschen Tuberkuloseschutzimpfverfahrens in der Praxis, Zentralbl. f. Bakteriologie, 1909, lii, 389.
188. Elkan, S.: Die Bedeutung des Tuberkulins im Kampf gegen die Tuberkulose, Berl. klin. Wchnschr., 1909, p. 104.
189. Ferreira, C.: L'Atoxyl dans la Tuberculose, Tuberkulosis, 1909, p. 63.
190. Fischer, B.: Histologische Untersuchungen über den Einfluss der Bierschen Stauungshyperämie auf die menschliche Tuberkulose, Frankfurter Ztschr. f. Pathol., 1909, p. 926.
191. Frugoni, C., and Grixoni, G.: Günstiger Einfluss der Wirksamen Elemente der Schilddrüse auf die experimentellen tuberkulösen und pseudo-tuberkulösen Infektionen, Berl. klin. Wchnschr., 1909, p. 1160.
192. Fuchs, A.: Ueber die Behandlung tuberkulöser Kinder mit hohen Tuberkulindosen, Verhandl. d. Ges. f. Kinderh., 1909.
193. Gabilowitsch, J.: Ueber das Endotin die wirksame Substanz des Kochschen Alttuberkulins, Tuberkulosis, 1909, p. 507.
194. Ganghofer, F.: Ueber die Behandlung tuberkulöser Kinder mit dem Antituberkuloseserum Marmorek auf rektalem Weg, Wien. klin. Wchnschr., 1909, p. 92.
195. Gasis, D.: Ein weiterer Beitrag zu meiner neuen Differentialfärbungsmethode der Tuberkelbazillen, Berl. klin. Wchnschr., 1909, p. 836.
196. Gudzent: Behandlung mit der Kuhnschen Lungensaugmaske, Berl. klin. Wchnschr., 1909, p. 201.
197. Häntjens, A.: Die Behandlung mit Filtrase, einem neuen Mittel gegen Tuberkulose und die damit erzielten Resultate, VIII intern. Tuberkulosekonferenz, 1909.
198. Hamman, L., and Wolman, S.: Tuberculin Treatment Among Dispensary Patients, Bull. Johns Hopkins Hosp., 1909, p. 225.
199. Henig, A.: Die Frühdiagnose der verschiedenen Tuberkuloseformen und der Einfluss der nordischen Meere auf Tuberkulose, Ztschr. f. Tuberk., 1909.
200. Herzberg, S.: Vorläufige Mitteilung über die Behandlung mit "JK" Spengler, München. med. Wchnschr., 1909, p. 243.
201. Karewski, F.: Ueber die neuen Methoden chirurgischer Therapie der Lungentuberkulose, Ztschr. f. Tuberk., 1909, p. 465.
202. Karo, W.: Spezifische Mittel in der Diagnose und Therapie der Urogenitaltuberkulose, VIII intern. Tuberkulosekonferenz, 1909.
203. Királyfi, G.: Ueber die Virulenzänderung der Tuberkelbazillen im Verlauf der spezifischen Behandlung, Ztschr. f. med. Klin., 1909, lxxvii, 141.
204. Klapp: Die konservative Behandlung der chirurgischen Tuberkulose, Deutsch. med. Wchnschr., 1909, p. 1739.
205. Klebs, E.: Die antagonistische Therapie der Tuberkulose, VIII intern. Tuberkulosekonferenz, 1909.
206. Koch, A.: Bemerkungen zur vorläufigen Mitteilung über die Behandlung mit "JK" von P. Herzberg, Ztschr. f. Tuberk., 1909, p. 213.
207. Köhler, F.: Behandlung der Lungentuberkulose an der See, Ztschr. f. Tuberk., 1909, p. 60.
208. Köhler: Beiträge zur stomachalen Anwendung der Kochschen Bazillenemulsion, Ztschr. f. Tuberk., 1909, p. 89.
209. Köhler: Die Bedeutung Agyptens in der Behandlung unserer Lungentuberkulösen, Ztschr. f. Tuberk., 1909, p. 390.
210. Köppler, K., and Neumann, W.: Opsonischer Index und Tuberkulosetherapie nebst Beiträgen zur Technik und Dosierung der Tuberkulininjektionen, Wien. klin. Wchnschr., 1909, p. 1547.
211. Kraus, H.: Zur Technik der Sonnenlichtbestrahlung der Kehlkopftuberkulose, München. med. Wchnschr., 1909, p. 658.
212. Krause: Interne Anwendung von Tuberkulin, Ztschr. f. Tuberk., 1909, p. 73.
213. Krokiewicz, A.: Ueber die Behandlung der Tuberkulose, Wien. klin. Wchnschr., 1909, pp. 301 and 340.
214. Lang, E.: Die Behandlung des Lupus vulgaris, mit Rücksicht auf die Pathogenese, Deutsch. med. Wchnschr., 1909, p. 1743.
215. Lissauer, A.: Zur Technik der Kehlkopfspiegelung mit Sonnenlicht, München. med. Wchnschr., 1909, p. 920.
216. Litzner: Ein Fall von Lupus des Gesichtes, behält mit Kochs Tuberkulin, Ztschr. f. Tuberk., 1909, p. 231.
217. Lütjhe: Einige Bemerkungen über die Bedeutung der Opsonine, speziell für die Diagnose und Therapie der Tuberkulose, Therap. Monatschr., 1909, p. 12.
218. Maltat, J.: Les énergies solaires dans la tuberculose pulmonaire, Tuberkulosis, 1909, p. 11.
219. Montenegro, V.: Sur les méthodes de traitement par la tuberculine, Ztschr. f. Tuberk., 1909, p. 129.
220. Most, A.: Ueber die Entstehung, Verhütung und die Behandlung der Halsdrüsentuberkulose, Berl. klin. Wchnschr., 1909, p. 93.
221. Most: Ueber den heutigen Stand der chirurgischen Behandlung der Lungentuberkulose, Tuberkulosis, 1909, p. 99.

222. Naumann, H.: Kreosot und Blutdruck, *Ztschr. f. Tuberk.*, 1909, p. 213.
223. Neumann, W.: Zur operativen Behandlung der Spondylitis tuberculosa, *Beitr. z. klin. Chir.*, 1909, lxx, 446.
224. Onodi: Ueber die chirurgische Behandlung der Nasenscheidenwandtuberkulose, VII. intern., Tuberkulosekonferenz, 1909.
225. Pannwitz, K.: Gesichtspunkte für den Bau und Betrieb einer Kinderheilstätte, VIII. intern., Tuberkulosekonferenz, 1909.
226. Pel, K.: Die Tuberkulinbehandlung der Lungentuberkulose, *Berl. klin. Wchnschr.*, 1909, p. 1717.
227. Röhrner: Anatomische Heilungsvorgänge der Lungentuberkulose des Säuglings, Verein Niederrh.-Westf.-Südwestd., Kinderärzte, 1909.
228. Rogatschewski: Knochen- und Gelenktuberkulose und ihre Behandlung mit homöopathischen Mitteln, St. Petersburg, Selbstverlag, 1909.
229. Rumpf, E.: Zweiter Jahresbericht von Dr. Rumpf's Sanatorium Ebersteinburg bei Baden-Baden, 1908, *Zeitschr. f. Tuberk.*, 1909.
230. Saathoff: Tuberkulindiagnostik und Therapie nebst Stoffwechselversuchen bei der Tuberkulintherapie, München. med. Wchnschr., 1909, p. 2041.
231. Saugmann, Chr.: Eine verbesserte Nadel zur Pneumothoraxbildung, *Ztschr. f. Tuberk.*, 1909, p. 223.
232. Schenker: Weitere Beobachtungen in der Tuberkulosetherapie bei Anwendung von Marmorek-Serum, München. med. Wchnschr., 1909, p. 174.
233. Schröder, G.: Ueber neuere Medikamente und Nährmittel für die Behandlung der Tuberkulose, *Ztschr. f. Tuberk.*, 1909, p. 501.
234. Schütz, A., and Vidéki, R.: Ueber die Behandlung der phlyktanulären Augenerkrankungen auf Grundlage ihrer Aetiologie, *Wien. klin. Wchnschr.*, 1909, No. 25.
235. Schultz, W.: Klinische Erfahrungen mit Eisentuberkulin., *Berl. klin. Wchnschr.*, 1909, p. 1721.
236. Selter: Einige Erfahrungen über den Spenglerschen Immunkörper bei der Tuberkulose, *Frankfurter Ztschr., f. Pathol.*, 1909, p. 926.
237. Sikemeyer, W.: Die Behandlung der chirurgischen Tuberkulose mit Marmorek-Serum, *Med. Klinik*, 1909, 1039.
238. Stock, W.: Ueber die Anwendung der Wrightschen Oponintechnik in der Augenheilkunde, speziell bei tuberkulösen Erkrankungen der Augen., *Monatschr. f. Augenheilk.*, 1909, p. 537.
239. v. Szabóky: Meine mit der C. Spenglerschen Behandlung erzielten Resultate, *Ztschr. f. Tuberk.*, 1909, p. 1.
240. Tarmann, J.: Ueber die Behandlung der Tuberkulose mit einem spezifische wirkenden Jodpräparat, München. med. Wchnschr., 1909, p. 1532.
241. Vos, H.: Ueber die rektale Anwendung des Marmorek-Serums in der Lungentuberkulose, *Ztschr. f. Tuberk.*, 1909, p. 346.
242. Weinberger: Zur Bezeichnung der Tuberkulindosen. München. med. Wchnschr., 1909, p. 2217.
243. Wolmann, S.: Marmorek Serum in the Treatment of Pulmonary Tuberculosis, *Bull. Johns Hopkins Hosp.*, 1909, p. 253.
244. Zeuner, W.: Spezifische Behandlung bei experimenteller Tuberkulose, *Zentralbl. f. Bakteriöl.*, 1909.

Tuberculin Therapy.—According to Lüthje²²⁷ the question whether the opsonic index should be followed in tuberculin therapy has not yet been answered; one can find definite indications for treatment in the clinical observations.

W. Stocks²²⁸ careful experiments have shown that an increase in the opsonic index does not mean that the patient is better. He believes, therefore, that it is quite unnecessary as a control for the tuberculin cure. Clinical observation alone is of value. Köpler and Neumann²²⁹ come to the same conclusion. Tuberculin therapy in children. Aronade²³⁰ warns against the use of tuberculin in infancy.

Röhrner²²⁷ did not think tuberculin treatment did harm in infancy, and he was able to demonstrate connective tissue surrounding a tuberculous center at an age in which such healing is very rare.

Schütz and Vidéki²³⁴ recommend tuberculin treatment in phlyctanulæ of tuberculous origin.

Fuchs¹⁹² speaks of the results of treating with tuberculin according to Schlossmann. The cases of bone, skin and lung tuberculosis in older children are noted. Injection in the neighborhood of the diseased joints caused an edema with large spots; repeated injection caused a picture which resembled erythema confusiforme.

Elkan¹⁸⁸ is an adherent of tuberculin therapy. In early cases cure may be expected with certainty and in advancing cases in which the patient is in tolerable general condition and without fever, the process will be stopped. He does not give any proof. Sahli is an adherent of tuberculin treatment with small doses, which give no reaction, and believes that the tuberculin treatment should be used, playing a "blessed part" in the question of tuberculosis, just as does vaccination in the fight against small-pox. However, he does not believe all patients should be treated with tuberculin. Turban discusses in detail the value

of tuberculin therapy in tuberculosis of the lungs. He is not convinced of the superiority of Beraneck's tuberculin over A.T. Rumpf²²⁹ did not always obtain good results from tuberculin therapy and he did not consider it necessary to inject all cases, but only those in which the condition in the lungs showed no further improvement. Saathoff²³⁰ observed gain in weight in 80 per cent. of the patients with tuberculin treatment and considered that the reaction to tuberculin made a considerable change in the mineral metabolism. He believed that the disease was favorably influenced by injections of one-fourth to one-half milligrams. The good results were most marked in a 13-year-old boy with glandular tuberculosis and a man aged 18 with disease of the conjunctival and nasal mucous membranes.

Bertarelli¹⁸⁵ found that immunizing doses of tuberculin in healthy men do not increase the agglutinins for the tubercle bacillus.

Litzner²¹⁶ cured a woman with tuberculin after she had been treated six months with the Finsen light without improvement. He began with 0.002 mg. old tuberculin and increased slowly up to 10 mg. in the course of 20 injections, and brought about a cure which was shown in the photograph accompanying the article.

Pel²²⁶ believes that the physician who does not treat pulmonary tuberculosis with tuberculin, does not commit a sin of omission, because this treatment is still in the experimental stage.

Herzberg²⁰⁰ maintains that he has cured an advancing pulmonary tuberculosis with Spengler's tuberculin in an extremely short time. Koch²⁰⁸ considers Herzberg's claims inexcusable.

Selter²³⁸ saw improvement in the general condition and diminution of the fever in external tuberculosis with the use of Spengler's immune bodies, but the results were not uniform when applied to the lesion itself. V. Szabóky²³⁹ saw improvement only when Spengler's method of vaccination was used in conjunction with climatic therapy. Kiralfi²⁰³ tested the virulence of the bacilli from the sputum of patients according to Spengler's method and found that with the progress of the treatment there were always insignificant changes in the animals experimented on and that after long-continued specific therapy the animals died of cachexia instead of tuberculous lesions. This phenomena disappeared if the treatment was discontinued or if the patients became worse under treatment.

Modifications of Tuberculin Therapy.—Zeuner²⁴⁴ treated tuberculous guinea-pigs with a modified tuberculin (oleic acid extract) with success. Häntjens¹⁹⁷ tried injections of the products of metabolism of living tubercle bacilli which were obtained by filtering through a filter. His results are similar to those of other writers who have used tuberculin. He never saw any harm from its use. Schultz²³⁵ used iron tuberculin with good results. Krokiewicz²¹⁸ injected thymol, hetol, stovain, atoxyl, gujasanol, and sodium chlorid at the same time with tuberculin. He speaks of the indications and contraindications and reports success.

Marmorek's Serum.—According to Schenker²²² it helped fifty patients with pulmonary tuberculosis in the first and second stages and mild grades of disease in bone, peritoneum, kidney and bladder. Pulmonary tuberculosis in the third stage improved. No harmful effects were noted. Sikemeier saw improvement in surgical tuberculosis. Vos²⁴¹ had the impression that it helped all patients with advanced tuberculosis. Ganghofer's²⁰⁴ experiences in his clinic led him to the conclusion that rectal administration of the serum was of doubtful value. According to Karo²⁰² the use of Marmorek's serum in urogenital tuberculosis is useless and dangerous. According to Turban the serum does not immunize, and may cause fever in mild cases and do harm by bacteriolysis in severe cases.

Active Immunization.—Bartel and Harth¹⁸² saw increased artificial resistance against tuberculosis in rabbits after intraperitoneal injections of emulsions of cultures. Bartel and Neumann¹⁸³ found that specific treatment with emulsions of tubercle bacilli caused an immunity in animals against tuberculosis.

Surgical Treatment.—Most²²¹ gave a synopsis of the *status quo* of the surgical treatment of pulmonary tuberculosis. Karewski²⁰¹ reported the indications of surgical treatment of phthisis. He speaks of the application of Freud's method of treatment. Neumann²²³ recommends drainage in spondylitis when there is abscess formation and lameness; laminectomy when there are secondary changes in the spinal canal and removing the cause. Lang²¹⁴ describes his radical treatment of lupus. Most²²⁰ recommends radical operation on tuberculous cervical glands when they do not disappear under conservative treatment, or if they show no spontaneous inclination of disappearing. Fischer¹⁹⁰ saw an increase in the inflammation in the tuberculous tissue with Bier's stasis, an increase in the leukocytes and infiltration with lymphocytes, and believes that this inflammation can result in absorption, cicatrization and encapsulation.

Klapp²⁰⁴ recommends operative interference in surgical tuberculosis only if the general condition shows severe damage (nephritis, amyloid, severe lung or intestinal tuberculosis) with the exception of those cases in which the smallest operative procedure cannot be borne. It is of most value in coxitis. He also considers operative treatment indicated when the local condition reacts on the whole body (mixed infection with hectic fever, especially in isolated extra-capsular foci with sequestrums). The conservative Bier treatment gives good results, especially in youth. He recommends along with this treatment mixed feeding, especially with meat; a vegetarian diet predisposes to tuberculosis. He had good results with Schrot's cure. He also had good results by applying trypsin to digest pus, and especially by injecting 60 per cent. alcohol in tuberculosis of the tendon sheaths and bursæ to stimulate the growth of connective tissue.

Medicinal Therapy.—Turmann²⁴⁰ MMW presumed that there was a specific action of iodine on the tuberculous focus, possibly by the chemical action of iodine on the albuminous bodies in the tubercle bacilli. He found that the preparation did well in guinea-pigs. The treatment of pulmonary tuberculosis and lupus followed.

Krause²¹² recommends anew the internal administration of tuberculin in the form of phytosoremid, along with and supplementary to the subcutaneous method.

Köhler²⁰⁸ denies that phytosoremid has no action, but in a large number of cases, no striking results can be seen. His observations are interesting, that there may be gain in body weight, even when the condition in the lungs progresses and the general condition does not improve. These observations are similar to those of Saathoff with subcutaneous injections of tuberculin.

Naumann²²² says that treatment with creosote does not increase a blood-pressure which is already high and believes that hemorrhages during such treatment is not the result of the creosote.

According to Frugoni and Grixoni¹⁹¹ treatment with thyroid gland should have a beneficial action on experimental tuberculosis in rabbits; in many instances the animals continued to live a long time.

Ferreira¹⁸⁹ reported good results from the injection of atoxyl. After a series of injections there was gain in weight, and improvement in the lungs as well as the general condition.

Physical and Dietetic Therapy.—Köhler²⁰⁷ recommends the seashore for the treatment of pulmonary tuberculosis.

Henig¹⁸⁹ believes that the temperature stimulatory climate of the east and north seas are more desirable in the early stages of pulmonary tuberculosis than the warmer south or the Riviera.

Köhler²⁰⁹ compiled the indications and contraindications of the treatment of tuberculosis in Egypt, on the basis of observations made by himself on the climatic conditions. He believes that Egypt will not be called to play a large rôle in the treatment of pulmonary tuberculosis among Germans.

Malgat²¹⁸ has seen good results in pulmonary tuberculosis from sun-baths—100 per cent. cure in mild cases, 65 per cent. in moderate, and 25 per cent. in severe.

Baradat²⁵¹ recommends the high altitudes of the province of St. Gervais.

Schenker²⁵² believes that fresh air and sun-baths are necessary and that misty regions in both summer and winter often give strikingly good results.

Kraus²⁵¹ has constructed a speculum for tuberculosis of the larynx with which the patient can throw the sunlight onto the larynx. Lissauer²⁵⁵ recommends throwing light on the patient by means of a mirror so that the duration and amount of exposure may be controlled.

Schutz and Vidéki²⁵⁴ handled phlyctenulæ which they did not consider tuberculous, but due to an "exudative" foundation, successfully with Czerny's diet. It does not make any difference whether the phlyctenulæ are tuberculous or not, the diet is a good one and results in improvement. This is easily understood because proper diet influences the course of the milder forms of tuberculosis.

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GASTRO-INTESTINAL SYSTEM

A Review of the Recent Investigations as to the Causes of "Summer Diarrhea" and Infant Mortality in Summer

1. Rietschel, Hans: Die Sommersterblichkeit der Säuglinge, *Ergbn. d. inn. Med. u. Kinderh.*, 1910, vi.

2. Holt, L. E.: Infant Mortality and Its Reduction, Especially in New York City, *Jour. Am. Med. Assn.*, 1910, liv, 682.

3. Heim, P., and John, M. K.: Die Thermoregulation des gesunden und ernährungs-gestörten Säuglings, *Jahrb. f. Kinderh.*, March, 1911, lxxiii, 266; quoted by Rietschel.

Included in the following bibliography are additional references which bear most directly on the subject treated on in this paper. For the complete list, as compiled by Rietschel, the reader is referred to his original article.

Baginsky: Ueber cholera infantum, *Berl. klin. Wehnschr.*, 1889, Nos. 46, 47, 48; Ueber der Durchfall und Brechdurchfall der Kinder, *Jahrb. f. Kinderh.*, 1875, viii; Ueber cholera infantum, *Arch. f. Kinderh.*, 1891, xii.

Ballard: Seventeenth Ann. Rep. Govt. Board, 1887-1888; Suppl. in Continuation of the Report of the Medical Officers for 1887, Diarrhea and Diphtheria, London, 1889.

Booker: A Bacteriological and Anatomical Study of the Summer Diarrheas of Infants, Baltimore, 1896; The Early History of the Summer Diarrhea of Infants, *Arch. Pediat.*, 1901, xviii.

Czerny and Moser: Klinische Beobachtungen an magendarmkranken Kindern im Säuglingsalter, *Jahrb. f. Kinderh.*, xxxviii.

Czerny and Keller: Des Kindes Ernährung, Ernährungsstörungen und Ernährungstherapie, Leipsic-Wien, 1901-09.

Engel-Bey: Statistique sanitaire des villes de l'Egypte 1886-1890; Mortalité des villes de la Basse-Egypte. La Caire, 1889; Welche Schlüsse ergeben sich aus der Säuglingsterblichkeit in bezug auf Wohnung und Ernährung? *Berl. klin. Wehnschr.*, 1907, No. 49.

Escherich: Die Aetiologie der primären Magendarmerkrankungen der Säuglinge bakteriellen Ursprungs, *Wien. klin. Wehnschr.*, 1900, No. 38; Beitrag zur Pathogenese der bakteriellen Magendarmerkrankungen der Säuglinge, *Verhandlung d. Gesellsch. f. Kinderh., Heidelberg*, 1889; Die Bedeutung der Bakterien in der Aetiologie der Magendarmerkrankungen der Säuglinge, *Deutsch. med. Wehnschr.*, 1898, Nos. 40 and 41; Ueber Streptokokkenenteritis im Kindesalter, *Jahrb. f. Kinderh.*, 1899, xlix; Ueber spezifische Krankheitserreger der Säuglingsdiarrhöen Streptokokkenenteritis, *Wien. klin. Wehnschr.*, 1897, No. 41; Die akuten Verdauungsstörungen im Kindesalter, *Deutsch. Klinik, Leyden*, 1902.

Finkelstein: Ueber Morbidität und Mortalität in Säuglings-spitälern und deren Ursacher, *Ztschr. f. Hyg. u. Infektionskrankh.*, xxviii; Ueber den Sommergipfel der Säuglingsterblichkeit, *Deutsch. med. Wehnschr.*, 1909, No. 32.

Flexner and Holt: Bacteriological and Clinical Studies of the Diarrheal Diseases of Infancy, from the Rockefeller Institute, 1904.

Flügge: Das Wohnungsklima zur Zeit des Hochsommers, Beitr. z. Hyg., Leipsic, 1879; Aufgaben und Leistungen der Milchsterilization, Ztschr. f. Hyg. u. Infektionskrankh., xvii.

Flügge, Paul, Ercklentz, Heymann: Ueber Luftverunreinigung, Wärmestauung und Lüftung in geschlossenen Räumen, Ztschr., f. Hyg. u. Infektionsk., xlix.

Fürst: Die Säuglingssterblichkeit in München in den Jahren 1895-1904, und Einfluss der Witterungsverhältnisse u.s.w., Deutsch. Vierteljahrsschr. f. öffentl. Gesundheitspfl., 1871.

Geigel: Die Kindersterblichkeit in Würzburg, Deutsch. Vierteljahrsschr. f. öffentl. Gesundheitspfl., 1871.

Geuersich: Der Einfluss der Wärme auf die Temperatur der Säuglings, Monatsschr. f. Kinderh., 1871.

Groth: Statische Unterlagen zur Beurteilung der Säuglingssterblichkeit in München, Ztschr., f. Hyg. u. Infektionskrankh., li.

Hammerl, Helle, Kaiser, Müller and Prausnitz: Sozialhygienische und bakteriologische Studien über die Sterblichkeit der Säuglinge, Arch. f. Hyg., lvi.

Heim and John: Ueber die interne Anwendung von Salzlösungen bei Behandlung der akuten Ernährungsstörungen im Säuglingsalter, Monatsschr. f. Kinderh., xlv.

Heller: Belehrung über Hitzschlag auf Märschen, Berlin, 1904.

Illoway: Die Aetiologie, Pathologie und Therapie der Sommerdiarrhoe der Kinder, Berlin, 1905.

Klose: Ueber den Sommertod der Säuglinge, Monatsschr. f. Kinderh., ix.

Langstein: Diskussion zum Vortrag "Ueber Kindermilch" in der Gesellsch. f. Kinderh., Breslau, 1904.

Liefmann: Die Bedeutung sozialer Momente für die Säuglingssterblichkeit, Ztschr. f. Hyg. u. Infektionskrankh., lxii.

Meinert: Die klinischen Bilder der die Kindersterblichkeit des Hochsommers beherrschenden Krankheitsformen, Verhandl. d. Gesellsch. f. Kinderh., Wiesbaden, 1887; Untersuchungen über den Einfluss der Lufttemperatur auf die Kindersterblichkeit u.s.w., Deutsch. med. Wehnschr., 1888; Ueber cholera infantum aestiva, Therap. Monatsh., 1891; Ueber die hohe Kindersterblichkeit der heissen Monate. Vortrag auf der Ausstellung von Erzeugnissen der Kindespflege gehalten, Dresden, 1895; Säuglingssterblichkeit und Wohnungsfrage, Arch. f. Kinderh., xlv; Bemerkungen zu der Erwiderung von Dr. J. K. Friedjung, Ebenda, xlv; Kindersterblichkeit und Milchversorgung der Städte Bericht über den 6 Verbandstag deutscher Milchhändler-Vereine, Berlin, 1907.

Peiper: Die Säuglingssterblichkeit in Pommern, Klin. Jahrb., xxiii.

Petruschky and Kriebel: Die Ursache der Sommersterblichkeit der Säuglinge und die Möglichkeit ihrer Verhütung, Leipsic, 1904; Weitere Studien zur Frage der Milchverderbnis als Ursache der Säuglingssterblichkeit, Leipsic, 1908; Diskussion zum Vortrag "Ueber Kindermilch," Verhandl. d. Gesellsch. f. Kinderh., Breslau, 1904.

Plaut: Einfluss der Beschaffenheit von Milch und Wohnung auf das Gedeihen der Ziehkinder in Leipsic Ztschr. f. Hyg. u. Infektionskrankh., xv.

Prausnitz: Physiologische und sozialhygienische Studien über Säuglingsernährung und Säuglingssterblichkeit, München, 1902; Ursachen und Bekämpfung der hohen Säuglingssterblichkeit, Vierteljahrsschr. f. öffentl. Gesundheitspfl., xxxiii.

Prausnitz and Kermauner: Statistik der Sterblichkeit der Säuglings an Magendarmkrankheiten, Jahrb. f. Nationalökon. u. Statistik, xiii.

Rietschel: Einige Bemerkungen über den Einfluss der Witterung auf die Säuglingssterblichkeit, Ztschr. f. Balneol., iii; Zur Aetiologie des Sommerbrechdurchfalls der Säuglinge, Monatsschr. f. Kinderh., ix; Die Ursachen der Sommersterblichkeit, Ztschr. f. Kinderschutz u. Jugendfürs., 2 Year, Nos. 8 and 9.

Rolly and Meltzer: Experimentelle Untersuchungen über die Bedeutung der Hyperthermie, Deutsch. Arch. f. klin. Med., xciv.

Rubner: Thermische Wirkungen der Luftfeuchtigkeit, Arch. f. Hyg., xii.

Rush: An Inquiry Into the Causes and Cure of Cholera Infantum, 1789.

Schlossmann: Studien zur Säuglingssterblichkeit, Ztschr. f. Hyg. u. Infektionskrankh., xxiv; Statistik und Säuglingssterblichkeit, München. med. Wehnschr., 1907.

Seibert: Cholera Infantum and the Weather, Med. Rec., New York, 1888, xxxiii.

Seiffert: Ueber die kulturelle und soziale Bedeutung der Kindersterblichkeit. Aus Saluti juventatis, Leipsic und Wien, Deuticke.

Thiemich: Ergebnisse der Säuglingsfürsorge. Part 3, Die Säuglingsfürsorge in Magdeburg, p. 33.

Willim: Säuglingssterblichkeit und Sommertemperatur, Ztschr. f. Hyg. u. Infektionskrankh., lxii.

Wunderlich: Das Verhalten der Eigenwärme in Krankheiten, Leipsic, 1868.

Würzburg: Die Säuglingssterblichkeit in Deutschland, Arbeit a. d. Kaiserl. Gesundheitsamte, ii and iv.

A recent article by Dr. Hans Rietschel¹ on the summer mortality in infants, contains an exhaustive review of this whole subject. To this communication is appended a careful bibliography. I wish at the outset to acknowledge my indebtedness to Dr. Hans Rietschel for a large part of the material contained in this paper.

Under the term "summer diarrhea" is included all those cases whose chief symptoms are diarrhea, vomiting, increase of temperature, loss of appetite, and some evident general disturbance of nutrition. These cases make up a large proportion of the deaths among infants from all causes during the summer months. Children of the class under consideration, dying with previous symptoms of intestinal disturbance, show at autopsy no definite lesions referable to the intestinal tract.

The class of cases under consideration in this paper is to be distinguished from two other groups of cases with severe diarrheal manifestations whose etiology is well known. These are cases of dysentery, the specific cause of which is the Shiga-kruze or the Flexner and streptococcus infectious (Escherich) bacillus. The Germans use the general term *Sommersterblichkeit* (summer mortality) to include those infants who die of diarrheal disease when no specific causes for these deaths can be ascertained. That term is obviously rather indefinite and corresponds closely with our conception of the term "summer complaint."

What is the underlying cause of the deaths, in summer, of infants whose chief symptom is diarrhea or some obvious disturbance of the gastro-intestinal tract?

Since the facts of bacteriology have become well-established an explanation of the cause of the great mortality among infants in summer has been sought either in the bacterial contamination of milk or some form of bacterial infection in the intestinal tract. To give weight to this point of view it is pointed out that breast-fed children are less liable to fall victims to summer diarrhea than are those artificially fed. These facts are well-known to everybody and have been generally accepted as satisfactory. The practical result of bacterial contamination of milk has found its expression in the establishment of milk depots for the dispensing of better milk and in the attempts to regulate the quality of the milk sold through dairies and stores.

Since, therefore, bacteria have been made responsible, either directly or indirectly, for this alarming mortality among infants, the questions arise, What bacteria are responsible for these results? and What are the toxic substances formed as a result of bacterial action which can explain these results?

The scope of this article will not admit of a discussion of the fundamental investigations of Escherich, Baginsky, Flügge, Czerny, Keller and others. The important facts to be noted here are that there has never been isolated any definite bacteria which can experimentally be proved to be the specific causes of the deaths resulting from summer diarrhea; that there has never been isolated from milk contaminated by bacteria any definite toxic substances whose effects on the organism can explain the large number of deaths from diarrhea in summer; and

that there has not been isolated from the stools of infants, bacteria which can experimentally be proved to be responsible for the deaths from summer diarrhea. An explanation of summer diarrhea or of the large infant mortality in summer on bacteriologic grounds is purely a hypothesis (Rietschel).

The point which Rietschel makes in his study of this subject is that bacterial decomposition of milk, or the effects of the action of bacteria in the intestinal tract may be a contributing cause to infant mortality in summer, but these alone are not sufficient to explain the great mortality among infants at that time.

There are certain other facts connected with the problem of summer diarrhea that have a directly important bearing on this subject. These matters have been commented on as far back in medical history as the late 18th century in this country (Rush), and more recently they have been made the subject of careful investigation abroad by Meinert, Rietschel, Finkelstein and others. If the interpretation which Rietschel places on these facts is correct, their bearing on summer diarrhea and the great mortality among infants in summer is a very important one.

The occurrence of summer diarrhea has a fairly well-defined geographical distribution. The countries in which it is most prevalent are America, England, France, the Netherlands, Germany, Austria-Hungary, Russia, the Balkan States, Greece, and, at times, Scandinavia. The farther north or the farther south one goes from these countries the lower is the summer mortality among infants. These countries present certain characteristics in common which are fairly definite. They are the countries in which industries have been most highly developed, where there has been the greatest centralization in large cities, and where there has been the greatest increase in artificial feeding. In these countries also there is a greater contrast in climatic conditions. The summer climate is relatively hot and the winter climate is relatively cold. It certainly is unfair to presuppose that the bacterial decomposition of milk is greater in these countries as compared with the other countries of the globe.

The question naturally arises as to what conditions prevail here to influence so unfavorably the infant mortality in summer as far as that is related to diarrheal diseases? In the countries in which summer diarrhea is most prevalent it is a well-known fact that there are more cases, and a higher mortality in cities than in the country. This relationship of summer diarrhea to cities is of considerable significance. It prevails to the greatest extent in large cities; it is greater in those cities where industries are more highly developed than in other cities; and it is concentrated in those sections of the large cities in which the population is congested and the conditions of existence are least satisfactory. Rietschel points out that the statistics for certain large industrial centers in Germany show no marked reduction of deaths in summer for the past two decades. In these centers of population, however, there have been important advances made in securing for the masses of the people a much purer milk-supply by means of sterilization, pasteurization, etc. In spite of these efforts to reduce the bacterial decomposition of milk the reduction in the summer death-rate has not taken place as had been hoped. In the statistics prepared by Holt² for New York City for a period extending from 1904 to 1908, inclusive, showing the mortality, by months, for infants under a year, there is seen no marked change in deaths during the summer months. These figures bear out, therefore, Rietschel's observations on that point with reference to the German cities.

It is well known to everybody that the largest number of deaths in summer among infants is among those who have previously suffered from serious digestive disturbances, or those whose digestions are below par. Any physician who has in charge children with feeble digestions fears for the welfare of these children during the summer months. This applies to children of the well-to-do as well as to the poorer classes. It is true, of course, that the latter infants are much more unfavorably affected than the former.

It is also significant that almost without exception a physician will advise parents to remove their children in summer from the city to the country, not-

withstanding the fact that they may go to some place where the milk-supply is less pure than that which they can obtain in the city.

At this point the question will naturally arise, What is the deleterious factor which affects so unfavorably in summer the artificially fed infants, especially those in congested industrial centers? Rietschel, Finkelstein and others answer that question by relating the high summer mortality to high temperatures, especially as they obtain in dwellings. The following facts are offered for consideration as bearing on this subject and as helping to offer a solution for the cause of summer deaths.

First of all, there is a direct relationship between the deaths among infants and the outside temperature. The number of infant deaths in summer increases directly with the increase in temperature. The figures in the accompanying table, collected by Seibert, and cited by Rietschel,¹ are instructive on this point.

TABLE SHOWING NUMBER OF DEATHS IN THE FIRST YEAR IN RELATION TO TEMPERATURES IN BERLIN

1895	—Average Maxi— mum Temp.		—Daily Mini— mum Temp.		Number of Deaths in First Year
	C.	F.	C.	F.	
May 19 to 25	20.6	69.08	8.5	46.30	166
May 26 to June 1....	24.1	75.38	11.7	53.13	195
June 2 to 8	22.7	72.86	13.	55.4	209
July 7 to 13	23.2	73.76	12.9	55.22	384
July 14 to 20	23.	73.4	12.9	55.22	399
July 21 to 27	25.9	78.62	15.9	60.62	450
July 28 to Aug. 3	25.3	77.54	16.	60.8	555
August 4 to 10	22.9	73.22	13.2	55.76	486
August 11 to 17	22.6	72.68	13.9	57.02	486
August 18 to 24	30.3	86.54	15.7	60.26	436

The close relationship between the increase in temperature and the increase in the number of deaths is clearly seen in the above table. An explanation for the apparent discrepancy in the figures August 18 to 24, as compared with those above them, may be found in the fact that although the maximum of the day-time temperature was excessively high at this time during August, thereby tending to increase the average maximum temperature for twenty-four hours, the nights were sufficiently cool so as to more than offset the effect of the high temperature during the day. Rietschel points out that the effects of heat are most damaging when it is continuous, with only slight variation of temperature between the night and the day, and when the heat is prolonged over a period of several days or weeks, even though the daily maximum temperature during this period may not itself be excessively high. Such a uniformly warm temperature gives no opportunity for the infant to "cool off," and the harmful effect of heat under these conditions reaches its maximum. The accompanying chart prepared by Finkelstein for Berlin for the year 1908 shows a comparison between the mortality among infants and the average daily temperature.

Finkelstein in analyzing this chart calls attention to two or three points of interest which are matters of frequent observation to physicians who are acquainted with heat conditions and deaths in the large cities.

1. By joining the lowest points of the curves it will be noted that there is a gradual rise in this broken line as the summer progresses; the interpretation of this will be discussed later.

2. By comparing the highest points of the daily temperature curve with the highest points of the mortality curve, it is seen that when the temperature goes above 20 degrees C. (68 F.) there is a marked increase in the number of deaths. This increase, however, reaches its maximum twenty-four hours after the temperature curve has reached its highest point. Whatever cause is at work here evidently works with remarkable quickness, so that between the life and death of

the infant only a short space of time intervenes. This relationship between the deaths and the temperature prevails whether it be in early, middle or late summer.

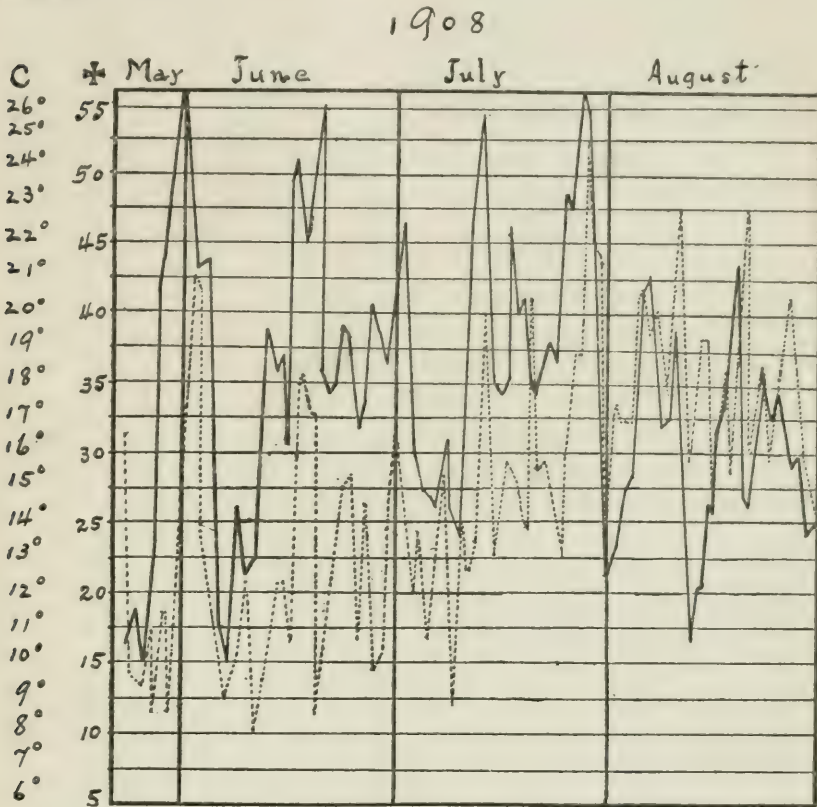


Chart showing the daily infant mortality during the summer of 1908 in the city of Berlin, compared with the average temperature (Finkelstein). The solid line indicates the average temperature; the dotted line, the infant mortality.

Does such a relationship exist between diseases caused by bad milk or by any form of contact infection? Assuming that contaminated milk may give rise to severe diarrhea in conditions of moderate temperature, it may be safely stated as a fact that the period between the sickness of the child and the child's death covers a considerable space of time. How many acute gastro-intestinal diseases are there which, as a result of bad milk, run such a fulminating course when the temperature of the air is not high, as is presented graphically in this chart? If the milk can be responsible for the condition represented in this chart, we must conceive that in the milk decomposition, substances of such extraordinary toxicity are formed as to produce fatal results within twenty-four or forty-eight hours. Such certainly is not the case in children with gastro-intestinal diseases at any other time than in the summer. According to Finkelstein, therefore, such diseases can only be explained by heat stroke or heat stasis. Experimentally and by experience it is well known that excessive heat is an agent that can cause death, if not in a few hours, at least in a few days. Instances are familiar to everybody of the effect of a high temperature produced artificially in infants as a result of hot water bottles, over-heated rooms, excessive clothing, etc. An infant, especially if he is subject to some chronic digestive disturbance or possesses a feeble resistance from other causes, if over-heated by hot water bottles, may show

an alarming hyperpyrexia, with symptoms of collapse, rapid breathing and even death, if there is no relief by energetic measures such as the use of hydrotherapy to reduce the temperature. The only causative factor of which we have definite knowledge that can produce such effects as are indicated in this chart is excessive heat.

How can it be explained, on the ground of milk contamination, that between the temperatures of 80 and 90 degrees F. the number of deaths is very markedly increased as a result of the ten point rise in temperature? Is it probable that ten degrees of temperature can make such a specific change in the milk as to cause that marked increase in the number of deaths?

Finkelstein explains the significance of the gradually ascending line which connects the lowest points of the mortality curve as follows: The line in the above chart which connects the lower points of the mortality curve represents those cases of infants who succumb to the effect of heat as it operates over a long period. There are a large number of infants who may not succumb to excessively high temperatures within a few hours, or a few days, but who cannot resist the continued effects of heat to which they are subjected over a period of weeks. These children clinically belong to the sub-acute and chronic types of diarrheal diseases, who as a result of prolonged heat stasis finally succumb to the deleterious effects of continued overheating. Finkelstein admits that his explanation of the significance of this gradually ascending base line is not altogether satisfactory. The explanation offered seems, however, to be as adequate as any that can be given.

Several observers have noted that, other things being equal, the mortality from diarrheal diseases, given a uniform heat, is increased if the air is comparatively calm, and that it is diminished if with this heat high winds prevail. The application of this fact to crowded tenements, narrow streets, and houses facing on courts in congested centers of population will become evident in discussing the relation of heat to dwellings.

It has already been stated, and is a matter of general experience, that the heat in cities is more dangerous to life than heat in the country. Laying aside the question of contamination of milk, two explanations for that fact may be found; first, in the prevalence of circulating air in the country as compared with the city, and secondly in the fall in temperature at night in the country as compared with the city. Cooler nights give a chance for the infant to combat to some extent the bad effects of excessive heat during the day. This advantage of course is not obtained in like degree by children or infants in the city, and especially those in the congested streets and dwellings.

The bad effects of heat not only reach their maximum in cities as compared with the country, but there is a concentration of this effect in certain definite districts and streets. The following figures for Dresden illustrate that point:

In 223 streets there were no cases of deaths in the midsummer period. In fifty streets 20 per cent., in sixteen streets 30 per cent. and in seven streets 40 per cent. of the infants living on those streets died in the midsummer period. The streets in which there were no deaths were situated in the higher parts of the city where there was better circulation of air, while in those streets where the mortality was greatest, there were greater congestion and less favorable conditions for the access of free air in dwellings (Weinert¹). Liefmann¹ made a careful study of this point with reference to Halle. His statistics are, however, too minute to introduce into this paper although they are of great interest in relation to this general topic. He found that in thirty-five streets alone, in Halle, there were 577 deaths of children in summer, while all the rest of the infant deaths, numbering 619, were distributed over 204 streets.

Where do the deleterious effects of heat show themselves to maximum advantage? The careful investigations of Rietschel and others answer this question definitely by saying that the heat in dwellings in summer months causes more disastrous results than in any other conditions. Over a period of five years Rietschel made a careful investigation of the heat in a large number of dwellings

in the congested districts of Berlin. These statistics show that the average heat of the dwellings which he made note of was several degrees higher than that of the outside air. This investigation was carried on with minute care as to accuracy of detail and must be accepted as representing the actual state of affairs. The limits of this paper do not allow of a presentation of his statistics and his method of investigation. These may be found out in an article by him in the *Zeitschrift für Kinderheilkunde*, March, 1911. His conclusions are that

In summer the harmful effects of heat find their chief significance in the direct influence of high temperature in dwellings, and the direct effect of heat on the child, especially as seen in dwellings, is the only causative agent that can satisfactorily explain the phenomenon of high summer mortality among infants. The conditions favoring this concentration of the effects of heat as found in dwellings in congested districts are as follows: The average temperature of dwellings is higher than that of the outside air in the congested districts of our large cities; the air in these dwellings is stagnant, i. e., there is little chance for circulation of air in crowded streets and courts, and consequently in the dwellings; the night temperature in these dwellings does not fall to the same extent as that of the outside air; and there are greater numbers of delicate infants, and children with digestive disturbances among those living in dwellings of this class. The contention may be made that these same conditions favor the bacterial decomposition of milk. Rietschel points out the fact that there may be a fall in temperature at night which is sufficient to diminish the injurious effects of the high temperature of the day-time, but which is not low enough to check the bacterial decomposition of milk. Although the child will continue to take bad milk the lower night temperature will diminish the death rate in spite of this.

In relation to the heat of dwellings, the following observations of Meinert are of considerable interest. He analyzed 580 cases of death from summer diarrhea with relation to the different floors on which these children lived. Of these died: In the basement or cellar, 3.982 per cent.; ground floor, 12.78 per cent.; first story, 10.7 per cent.; second story, 9.13 per cent.; third story, 8.18 per cent.; fourth story, 9.18 per cent.; fifth story, 11.27 per cent.

He explains this as follows: The low mortality in the basement is due to the fact that the air is much cooler there, notwithstanding the fact that it is especially unhealthy. As to the high mortality on the ground floor, the circulation of air is much less there than higher up in the building, and in addition the ground floor is exposed to the reflected heat from the pavement.

The gradually diminished mortality in the second and third stories may be explained as a result of the increasing effects of the circulation of air in these stories.

The increase in the mortality on the top story is the result of the excessive heat on account of its situation directly under the roof. This overheating more than offsets any advantage that might be obtained from the increase in the circulation of air in the top story.

Perhaps one of the strongest arguments in support of the bacterial decomposition of milk, or of bacterial infection of some sort in the causation of summer diarrhea is that artificially-fed children are more subject to diarrheal diseases than are breast-fed children. Now the question arises, Is there any explanation for this fact on any other than bacteriological grounds? Breast-milk is an infant's natural food, to which its digestion is naturally adapted. Any other form of food, notwithstanding the fact that it may be free from bacteria, is an unnatural form of nourishment for the child. In order to adapt such nourishment to the infant it is necessary to use extreme care in modifying it to the child's digestive capacity. It is well-known to everyone that, among the artificially-fed infants living in dwellings in the congested districts of our cities, there is a larger proportion of infants suffering from derangements of digestion, of greater or less degree, because of the lack of knowledge as to how properly to feed them. Given then, a large number of infants whose digestions are below par, or whose digestions are distinctly impaired, does high temperature have a

peculiarly deleterious effect on them as compared with breast-fed infants? Rietschel gives experimental proof to the effect that infants suffering from digestive disturbances react with a rise of temperature if the outside temperature is high more readily than do healthy infants. One of his methods of proof was as follows: He subjected infants, both healthy and those suffering from intestinal diseases, to high room temperatures for shorter or longer periods. The infants suffering with intestinal diseases reacted with higher temperatures than did those who were healthy. In some instances this sojourn in overheated rooms has excited symptoms of severe diarrhea in those children. In all of these cases the diet was free from any objection as far as bacterial contamination was concerned. The inference from these observations as it relates to the effect of summer heat in dwellings on children who were previously diseased, is clear.

If these children are now subjected to the high temperature of summer, especially as it prevails in dwellings, the effect of the excessive heat itself, without regard to any other causative factor, is sufficient to excite severe manifestations of summer diarrhea, and unless such children are removed to a cooler environment the overheating will probably be the cause of their death in large numbers.

The following question in connection with this immediate topic suggests itself. If the choice were given to treat a certain number of infants suffering from diarrheal diseases in summer during a period of excessive heat, either by furnishing these infants with a germ-free diet in their own dwellings, thereby not removing them from the heat, or by sending these same children to the country where the days and nights are comparatively comfortable, maintaining the same dietary conditions as prevailed in their own homes, which of the two courses would be chosen by the majority of physicians?

Rietschel, with a view of determining the effects of contaminated milk tried the following experiment. He allowed milk to stand in an open vessel in a room where the temperature was uniformly high, for a period of twenty-four hours. He then gave this soured milk to a considerable number of infants, some of whom were healthy and some of whom were suffering from intestinal diseases. The majority of healthy children were unaffected by it and a few showed slight disturbances of digestion. The symptoms of the children suffering from intestinal diseases were in some instances aggravated, but in no case was any serious disturbance excited, at least comparable to the manifestations which are seen in the typical summer diarrhea.

At this point, a few facts may be stated regarding the effect of heat on breast-fed children. There is no question but that they are better able to resist the effects of heat than are artificially-fed children. Rietschel cites instances from numerous observers that during a period of excessive heat in summer there has been a considerable number of breast-fed infants who have been the victims of severe summer diarrhea. These observations can be confirmed by many physicians who have been practicing among children. Rietschel³ quotes Engel Bey's observations on the high summer mortality in the lower Egyptian cities. This author states that in Cairo there is a high summer mortality among infants although the majority of infants are breast-fed. He has observed that this high mortality is found largely among those infants who live in dwellings in the congested sections of the city. He concludes that the high temperatures, especially as they obtain in poorly ventilated dwellings, is the direct cause of this mortality.

After putting together all the facts which have so far been advanced regarding the deleterious effects of summer heat, especially as it obtains in closely crowded dwellings, the question will naturally be asked, What is the specific nature of the effects of heat upon the organism? That question at present admits of no definite answer.

There are two types of heat effect: One is seen in what is called "heat-strokes;" the other is seen in the effects of prolonged high temperatures, resulting in what is called "heat-stasis." The effects of heat-stroke are familiar to everybody. It is well-known that excessive heat is directly responsible for the death

of a considerable number of adults in summer, and that its effect may operate within a period of a few hours, or at most two or three days. That heat-stroke is responsible for the death of a considerable number of infants, without relation to any other factor, must be admitted without question. In heat-stasis the nature of the pathologic process admits of no definite proof. High temperatures furnish an environment for the infant which does distinct harm to its general condition. Infants subjected to high temperatures react with an increase in their own body temperatures. The cause of the increased body temperature is explained as follows: When the surrounding temperature is high there is a disturbance in heat loss, and the failure of the child to lose body heat is the cause of the increase in body temperature. There is, in other words, heat stasis. This has been shown to be especially true of those whose constitutions are naturally delicate although not suffering from disease. This prolonged increase of body temperature, especially when it is continued for a period of days and weeks lowers the child's vitality in general and makes a demand on the body cells to functionate under abnormal conditions. The processes of metabolism take place, therefore, abnormally, and by some it is supposed that as a result of this perversion of the metabolic processes certain products are formed which are distinctly injurious to the child. L. F. Meyer advances the theory that in these children there is a salt-retention and that as a result of this retention the temperature of the child is raised. Rietschel concludes that the heat stasis which arises in an environment of high temperature, especially in dwellings, is more largely responsible in impairing the digestive functions than is contaminated milk.

Frequently it is seen that children suffering from the effects of summer diarrhea show striking improvement within a few hours if these children are removed to the country or spend twenty-four or forty-eight hours on one of our floating hospital ships down the bay. The practical question now arises, What can be done for the babies in our large cities to reduce the occurrence of summer diarrhea and the all too frequent deaths resulting from this condition?

Large sums of money have been spent in the past in the establishment of milk depots throughout the congested centers of population in New York and other large cities. The prime purpose of these milk stations has been to furnish pure milk to the poor. The efforts in the improvement of the milk-supply should be continued, as it is the plain duty of humanity to give babies the purest food that can be obtained. The results of these efforts toward the reduction of summer diarrhea and infant mortality are, however, limited. Keller, who is an advocate of the theory that contaminated milk is largely responsible for summer diarrhea, has admitted that the milk depots have not fulfilled their purpose. His disappointment in the good results he had hoped for from the general use of pure milk arose from the fact that there were so many victims of acute diarrhea among children who had been fed on sterilized or other unobjectionable milk. Thiernisch, in discussing the value of milk depots, is inclined to ascribe as much importance to the instructions given in the milk stations as to how to take care of babies in hot weather, as to the pure milk furnished by these depots.

Unless further effort is exerted to mitigate the effect of summer heat, the occurrence of summer diarrhea and the high summer mortality among infants will continue unabated. The problem, therefore, becomes, in part, one which has to be solved by the municipality. As long as the overcrowded tenements, situated on narrow streets or on courts, continue to exist, no amount of germ-free milk can offset the direct damage of the bad, stagnant air and excessive heat of dwellings in congested tenement districts.

The problem is obviously a very difficult one to solve. It is not a simple matter to pull down and destroy the thousands of unsanitary, badly ventilated dwellings in the congested sections of our cities. Something can be done, however, in obtaining for the infants in these dwellings more fresh air by removing them in larger numbers from their homes to the country or to the seashore during the heated time. The opportunity for philanthropy to do a work which is distinctly worth while can find unlimited range for its activity by furnishing

places of refuge for infants and children outside of the city during the hot months.

In the treatment of summer diarrhea every effort should be made to lessen as far as possible the overheating of the child. The preventive measures which are at our command group themselves roughly into two classes.

1. Removal of the child from overheated dwellings to the country or seashore.

2. The application of artificial means to prevent heat-stroke or heat-stasis in the dwellings themselves.

The more frequent use of cool baths or cool spongings to these infants and children who must remain at home during the heated period should be insisted on. If the child should receive tepid baths or spongings at a temperature of 70 to 80 F. every hour or two during the day and two or three times during the night, there is reason to believe that the injurious effects of heat would be remarkably diminished. The results which have been obtained in the use of tepid baths and packs in the treatment of acute attacks of diarrhea, especially in cholera infantum, when this is accompanied by high temperature, have been most satisfactory. It is important that the temperature of the water in case baths are given should be between 80 and 86 F. These should be repeated every hour or two, according to indications. Wet packs may be substituted for baths in the treatment of this condition, the temperature of the pack being from 60 to 70 F. This may be applied every half hour to every hour at the start, gradually increasing the intervals at which they are used.

Plenty of water should be given to drink within the first twenty-four or forty-eight hours of an acute attack. Some writers advise the administration of .3 per cent to .5 per cent. salt water instead of plain water for these cases. If there is repeated vomiting the salt water may be given subcutaneously or by rectum.

The dietetic and medicinal treatment which is required for these forms of summer diarrhea are treated fully in modern text-books on diseases of children.

In view of the present discouraging condition in the reduction of summer mortality any new point of attack which promises diminution in the occurrence of summer diarrhea will be welcomed. If the direct effect of heat is as harmful to the child, as some of the modern investigators believe, the opportunity to solve the problem from this point of view affords a promising field for future efforts.

F. H. BARTLETT.

DISEASES OF THE BLOOD

The Fever Curve in Splenic Anemia Due to Leishman's Parasite

(*C. Di Cristina: Rev. d'Tyg. et de méd. Infat., 1911, x, No. 1, p. 46*)

Ten cases of splenic anemia due to *Leishmania infantum* are reported, with histories and temperature charts, from Jemma's clinic in Palermo. These charts show a very irregular temperature-curve, sometimes of the intermittent, and sometimes of the remittent type. This irregularity is so constant that Di Cristina believes it to be of considerable diagnostic importance, as in no other disease is the change from one type to the other so rapid. The duration of the rise in temperature is usually short, and may be so short that several such elevations may occur in the same day, another characteristic found in no other disease.

J. HERBERT YOUNG.

GENITO-URINARY SYSTEM

Infection of the Urinary Tract in Children by Coliform Organisms

(W. M. Jeffreys: *Quart. Jour. Med.*, 1911, iv, 267)

Among 121 cases of infection of the urinary tract in children collected and studied by Jeffreys, sixty-seven were due to coliform organisms, thirty-seven to staphylococcus, ten to streptococcus, three to pneumococcus and four to other organisms. Of fourteen cases occurring during 1910, five patients died of the disease and one of meningococcal meningitis, in which the coli infection was a complication. There were sixteen cases in 1909, twelve cases in 1908, and nine cases in 1907; the remaining nine cases were scattered over the previous six years, and one of the patients died of the disease in 1905. Only ten dated the trouble from some previous illness, generally an acute specific fever. In thirty-four cases there was definite evidence of bowel trouble of one kind or another, in ten cases the bowels were noted as regular, and in sixteen there was no evidence pointing to bowel trouble. With regard to the chief symptoms complained of, in thirty-seven cases they pointed to bladder trouble, usually painful micturition; three cases were brought up for diarrhea and vomiting, nine for abdominal pain, five with meningeal symptoms, four for debility and in two there were no symptoms. Four cases were discovered in children suffering from some other illness. Twenty-one began with symptoms pointing to bladder trouble and nine with symptoms suggesting pyelitis. In thirty cases there was no evidence to suggest the mode of onset. There was evidence pointing to pyelitis in thirty cases; in twelve the right kidney only was affected, in three the left only. The renal trouble began in or was confined to the right kidney in seventeen cases, the left in five; in one of the latter the right kidney was more markedly affected than the left. In eight cases there was no evidence to show which kidney was first affected. Examination of the urine showed that pus was present in nearly every instance, fifty-six out of sixty. Albumin was present in forty-five and blood in fifteen. The urine was acid in thirty-nine cases, alkaline in seven, neutral in one and in the remaining thirteen cases no note was made of the reaction. Casts were noted as being present four times. Only twenty-one were discharged as being cured, that is to say, with no symptoms and no pus in the urine. Nine died; of these, six died of the urinary trouble and three of some other disease, of which the urinary infection was a complication. Six were discharged *in statu quo ante* and twenty-three as "improved"; this usually meant that symptoms had abated but that pus was still present in the urine. Altogether fourteen patients were untreated, except by rest in bed and nursing; of these, one was cured, five went out unchanged, two were "improved", and six died, three of the latter from some other complaint. Forty-six cases were treated with drugs, or local applications to the bladder, and twenty of them were cured, four with washing out the bladder, one with alkalis by the mouth, five with antiseptics by the mouth and one with vaccines. The remainder had various combinations of the above methods. The usual treatment was on three lines: 1. Alkalis. 2. Urinary antiseptics. 3. Local treatment to the bladder. These were usually combined. Jeffreys thinks it most important to treat the bowel condition by washing out the large intestine and keep it acting by means of aperients, but being careful not to produce further irritation of the large intestine, as is very likely with aperients. Judging by three patients cured by appendectomy, it seems well worth while resorting to this measure in stubborn cases.

F. C. Z.

THE NERVOUS SYSTEM

Influence of Salicylates on the Cardiac Lesions of Chorea

(E. A. Cockayne: *Quart. Jour. Med.*, iv, 336)

The records of 780 hospital patients with chorea treated during the last eight years were carefully examined by Cockayne in order to discover whether salicylates really have the power of preventing the onset of carditis, or, if

already present, of checking its further progress. Of the 780 patients, 355 were given salicylates and 425 received other treatment; 156 received doses below 60 gr. a day, 95 between 60 and 100 gr., 60 between 100 and 200 gr., 19 between 200 and 300, and eight, doses of more than 300 gr. a day, and the remaining patients were treated with aspirin. If the drug has no effect the numbers showing cardiac change should be in the proportion of thirty-nine untreated to thirty-two treated with salicylates, and the actual numbers obtained are so near these that the disparity can have no significance. It might be thought that the larger doses would have had more effect in preventing the progress of the cardiac trouble, but the statistics do not suggest that the size of the dose has any such effect. Cockayne assumes that the organisms of rheumatism were probably present in the myocardium, endocardium or pericardium in these cases, and the salicylates (in the doses usually given) appear to have had no action in preventing their entrance into the heart, nor in stopping their further activity when once established there. This is confirmed by their inability to check the continuance of that low, intermittent fever, with its daily or almost daily rise, usually to some point between 99 and 100 F., so characteristic of rheumatic infection in childhood. The fact that they do not prevent the formation of subcutaneous nodules, and that they have no action on choreic movements, which is probably due to toxins elaborated by organisms lying near the blood-vessels of the cerebrum, and poisoning the nerve cells in their vicinity, would lead one to expect by analogy that they would have no action in the similar conditions found in the heart, and Cockayne's results show that this is the case.

F. C. Z.

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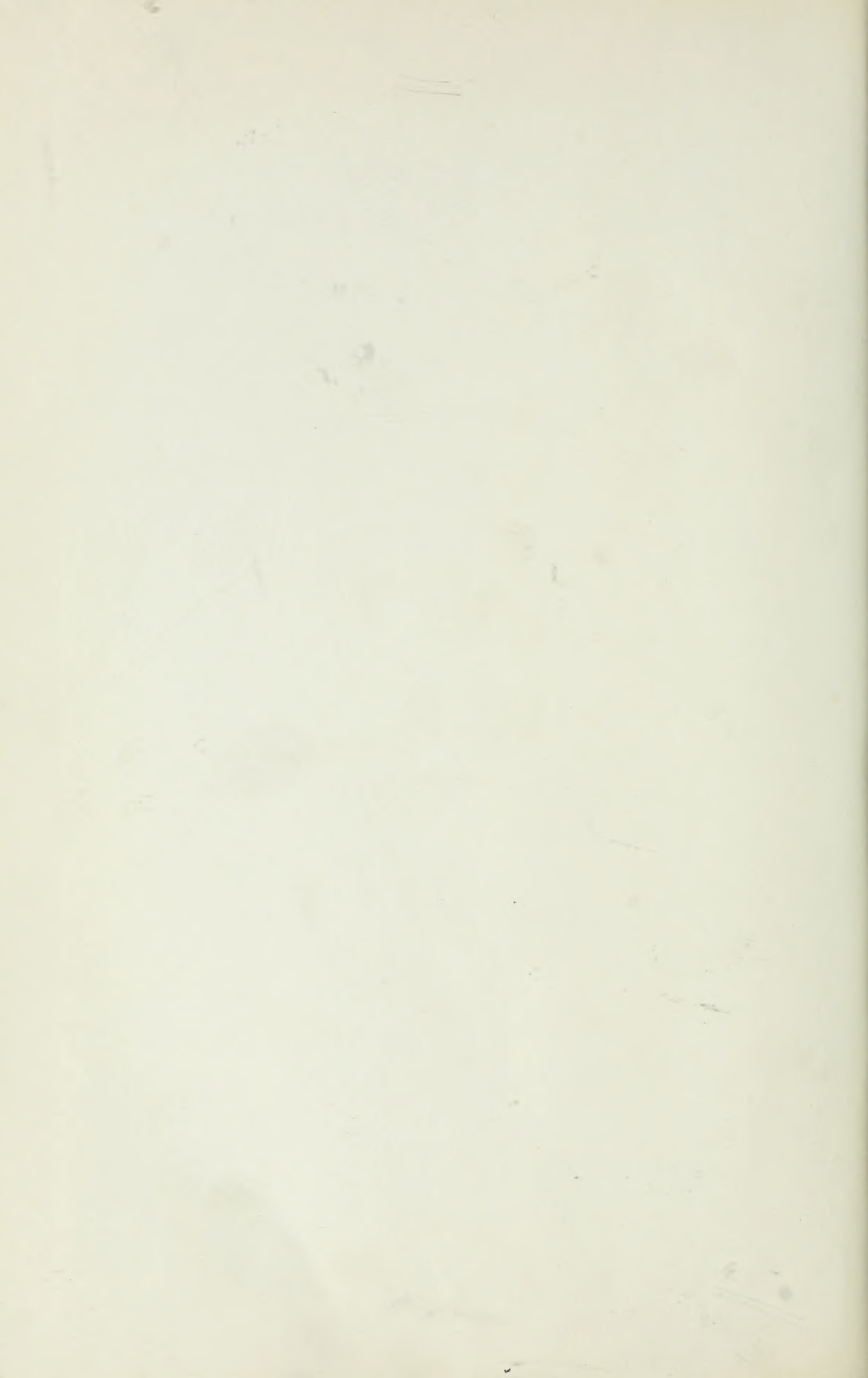
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